

U.S. Appl. No. 09/928,242
Response to Office Action Mailed 7/7/03
Page 4 of 93

AMENDMENT TO THE CLAIMS

▪ Format of Claim Amendments

Applicant has amended the claims as indicated below. Pursuant to the revised format to 37 C.F.R. 1.121 which is planned to be officially adopted by the USPTO in July of 2003, and which is now permitted by the office pursuant to the USPTO's release of January 31, 2003, Applicants herein submit only one version of the claims with markings to show changes. A detailed listing of all claims that are, or were in the application, are presented.

▪ Statement with Respect to Scope of Amended and Non-Amended Claims

Amendments to, cancellation of, and additions to, the claims are made in order to streamline prosecution of the case to embodiments that are presently anticipated to be of commercial significance, and are not made for a purpose of patentability. Any amendment, cancellation or addition made herein should not be construed in any manner as indicating Applicants' surrender of any subject matter of the application, or surrender of any equivalent to any element asserted in one or more claims. Applicants do not concede that the scope of the claims set forth below fail to extend as far as the original claims. Furthermore, any narrowing which may be evinced with respect to subject matter covered by the claims as a whole, or by one or more claims of the appended claims, when compared to claims previously in the application, should not be interpreted as indicating that the Applicants have generally disclaimed the territory between the original claimed subject matter and the amended claimed subject matter. Applicants intend each term of the claims set forth below to be read with respect to the full-breadth of the language of the claims and not to be confined to a strict literal read of amended terms. Amended claims elements are to be construed to include substantial equivalents known to those of ordinary skill in the art. Applicants assert that the amendments are made without prejudice and reserve all rights to prosecute any canceled claims, and claims preceding any amendment, and other disclosed (but not presently claimed) embodiments in the application, in future continuation applications, divisional applications, continuation-in-part applications,

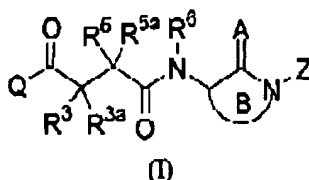
U.S. Appl. No. 09/505,788
Response to Office Action Mailed 12/12/02
Page 5 of 93

continuing prosecution applications, requests for continuing examination, re examination applications and any other application claiming priority from or through the present application.

**COMPLETE LIST OF CLAIMS THAT ARE OR HAVE BEEN BEFORE THE
OFFICE AFTER ENTRANCE OF THE AMENDMENTS MADE HEREIN
(See next page)**

U.S. Appl. No. 09/505,788
 Response to Office Action Mailed 12/12/02
Page 6 of 93

1. (CURRENTLY AMENDED) A compound of Formula (I):



or a pharmaceutically acceptable salt thereof, wherein:

A is O or S;

Q is $-NR^1R^2$;

R^1 is selected from: H and C₁-C₆ alkyl;

R^2 is independently selected from H and C₁-C₆ C₁-C₆ alkyl;

R^3 is $-(CR^7R^7a)_n-R^4$,

$-(CR^7R^7a)_n-S-(CR^7R^7a)_m-R^4$,

$-(CR^7R^7a)_n-O-(CR^7R^7a)_m-R^4$,

$(CR^7R^7a)_n-N(R^7b)-(CR^7R^7a)_m-R^4$,

$-(CR^7R^7a)_n-S(=O)-(CR^7R^7a)_m-R^4$,

$(CR^7R^7a)_n-S(=O)_2-(CR^7R^7a)_m-R^4$,

$-(CR^7R^7a)_n-C(=O)-(CR^7R^7a)_m-R^4$,

$(CR^7R^7a)_n-N(R^7b)-C(=O)-(CR^7R^7a)_m-R^4$,

$-(CR^7R^7a)_n-C(=O)-N(R^7b)-(CR^7R^7a)_m-R^4$,

$-(CR^7R^7a)_n-N(R^7b)-S(=O)_2-(CR^7R^7a)_m-R^4$, or

$-(CR^7R^7a)_n-S(=O)_2-N(R^7b)-(CR^7R^7a)_m-R^4$;

n is 0, 1, 2, or 3;

m is 0, 1, 2, or 3;

U.S. Appl. No. 09/505,788
Response to Office Action Mailed 12/12/02
Page 7 of 93

R^{3a} is H, OH, C₁-C₄ alkyl, C₁-C₄ alkoxy, C₂-C₄ alkenyl
or C₂-C₄ alkenyloxy;

R⁴ is H, OH, OR^{14a},
C₁-C₆ alkyl substituted with 0-3 R^{4a},
C₂-C₆ alkenyl substituted with 0-3 R^{4a},
C₂-C₆ alkynyl substituted with 0-3 R^{4a},
C₃-C₁₀ carbocycle substituted with 0-3 R^{4b},
C₆-C₁₀ aryl substituted with 0-3 R^{4b}, or
5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen,
oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with
0-3 R^{4b};

R^{4a}, at each occurrence, is independently selected from H, F, Cl, Br, I, CF₃,
C₃-C₁₀ carbocycle substituted with 0-3 R^{4b},
C₆-C₁₀ aryl substituted with 0-3 R^{4b}, or
5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen,
oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with
0-3 R^{4b};

R^{4b}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO₂,
NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(=O)CH₃, S(=O)₂CH₃,
C₁-C₆ alkyl, C₁-C₄ alkoxy, C₁-C₄ haloalkyl,
C₁-C₄ haloalkoxy, and C₁-C₄ haloalkyl-S-;

R⁵ is H, OR¹⁴,
C₁-C₆ alkyl substituted with 0-3 R^{5b},
C₁-C₆ alkoxy substituted with 0-3 R^{5b},
C₂-C₆ alkenyl substituted with 0-3 R^{5b},
C₂-C₆ alkynyl substituted with 0-3 R^{5b},
C₃-C₁₀ carbocycle substituted with 0-3 R^{5c},
C₆-C₁₀ aryl substituted with 0-3 R^{5c}; or

U.S. Appl. No. 09/505,788
Response to Office Action Mailed 12/12/02
Page 8 of 93

5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{5c};

R^{5a} is H, OH, C₁-C₄ alkyl, C₁-C₄ alkoxy, C₂-C₄ alkenyl, or C₂-C₄ alkenyloxy;

R^{5b}, at each occurrence, is independently selected from:

H, C₁-C₆ alkyl, CF₃, OR¹⁴, Cl, F, Br, I, -O, CN, NO₂, NR¹⁵R¹⁶;

C₃-C₁₀ carbocycle substituted with 0-3 R^{5c};

C₆-C₁₀ aryl substituted with 0-3 R^{5c}; or

5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{5c};

R^{5c}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO₂,

NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(=O)CH₃, S(-O)₂CH₃,

C₁-C₆ alkyl, C₁-C₄ alkoxy, C₁-C₄ haloalkyl,

C₁-C₄ haloalkoxy, and C₁-C₄ haloalkyl-S-

R⁶ is H;

C₁-C₆ alkyl substituted with 0-3 R^{6a};

C₃-C₁₀ carbocycle substituted with 0-3 R^{6b}; or

C₆-C₁₀ aryl substituted with 0-3 R^{6b};

R^{6a}, at each occurrence, is independently selected from H, C₁-C₆ alkyl, OR¹⁴, Cl, F, Br, I, -O, CN, NO₂, NR¹⁵R¹⁶, aryl or CF₃;

R^{6b}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO₂,

NR¹⁵R¹⁶, CF₃, C₁-C₆ alkyl, C₁-C₄ alkoxy, C₁-C₄ haloalkyl, and C₁-C₄ haloalkoxy;

R⁷, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO₂, CF₃, phenyl and C₁-C₄ alkyl;

U.S. Appl. No. 09/505,788
 Response to Office Action Mailed 12/12/02
Page 9 of 93

R^{7a}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO₂, CF₃, and C₁-C₄ alkyl;

R^{7b} is independently selected from H and C₁-C₄ alkyl;

Ring B is a 7 membered lactam or thiolactam,

wherein the lactam is 2-oxo-azepinyl or thiolactam is 2-thioxo azepinyl;

wherein each additional lactam carbon or thiolactam carbon is substituted with 0-2 R¹¹;
 provided two R¹¹ substituents are present on adjacent atoms and are combined to form a benzo fused radical; wherein said benzo fused radical is substituted with 0-4 R¹³;

and,

wherein the lactam or thiolactam contains a heteroatom selected from -N=, -NH-, and -N(R¹⁰);

R¹⁰ is H, C(=O)R¹⁷, C(=O)OR¹⁷, C(=O)NR¹⁸R¹⁹,
 S(=O)₂NR¹⁸R¹⁹, S(-O)₂R¹⁷;

C₁-C₆ alkyl optionally substituted with 0-3 R^{10a};

C₆-C₁₀ aryl substituted with 0-4 R^{10b};

C₃-C₁₀ carbocycle substituted with 0-3 R^{10b}; or

5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{10b};

R^{10a}, at each occurrence, is independently selected from H, C₁-C₆ alkyl, OR¹⁴, Cl, F, Br, I, -O, CN, NO₂, NR¹⁵R¹⁶, CF₃, or aryl substituted with 0-4 R^{10b};

R^{10b}, at each occurrence, is independently selected from H, OH, C₁-C₆ alkyl, C₁-C₄ alkoxy, Cl, F, Br, I, CN, NO₂, NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(-O)CH₃, S(-O)₂CH₃, C₁-C₆ alkyl, C₁-C₄ alkoxy, C₁-C₄ haloalkyl, C₁-C₄ haloalkoxy, and C₁-C₄ haloalkyl S;

R¹¹, at each occurrence, is independently selected from

U.S. Appl. No. 09/505,788
 Response to Office Action Mailed 12/12/02
Page 10 of 93

H, C₁-C₄ alkoxy, Cl, F, Br, I, CN, NO₂, NR¹⁸R¹⁹, C(=O)R¹⁷, C(=O)OR¹⁷,
 C(-O)NR¹⁸R¹⁹, S(-O)₂NR¹⁸R¹⁹, CF₃;
 C₁-C₆ alkyl optionally substituted with 0-3 R^{11a};
 C₆-C₁₀ aryl substituted with 0-3 R^{11b};
 C₃-C₁₀ carbocycle substituted with 0-3 R^{11b}; or
 5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen,
 oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with
 0-3 R^{11b};

R^{11a}, at each occurrence, is independently selected from
 H, C₁-C₆ alkyl, OR¹⁴, Cl, F, Br, I, -O, CN, NO₂, NR¹⁵R¹⁶, CF₃;
 phenyl substituted with 0-3 R^{11b};
 C₃-C₆ cycloalkyl substituted with 0-3 R^{11b}; and
 5 to 6 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen,
 oxygen, and sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-
 3 R^{11b};

R^{11b}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO₂,
 NR¹⁵R¹⁶, CF₃, acetyl, SCII₃, S(=O)CH₃, S(-O)₂CH₃.
 C₁-C₆ alkyl, C₁-C₄ alkoxy, C₁-C₄ haloalkyl,
 C₁-C₄ haloalkoxy, and C₁-C₄ haloalkyl-S-;

Z is H;
 C₁-C₈ alkyl substituted with 1-3 R¹²;
 C₂-C₄ alkenyl substituted with 1-3 R¹²;
 C₂-C₄ alkynyl substituted with 1-3 R¹²;
 C₁-C₈ alkyl substituted with 0-3 R^{12a};
 C₂-C₄ alkenyl substituted with 0-3 R^{12a};
 C₂-C₄ alkynyl substituted with 0-3 R^{12a};
 C₆-C₁₀ aryl substituted with 0-4 R^{12b};
 C₃-C₁₀ carbocycle substituted with 0-4 R^{12b}; or

U.S. Appl. No. 09/505,788
Response to Office Action Mailed 12/12/02
Page 11 of 93

5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{12b};

R¹², at each occurrence, is independently selected from
C₆-C₁₀ aryl substituted with 0-4 R^{12b};
C₃-C₁₀ carbocycle substituted with 0-4 R^{12b}; or
5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{12b};

R^{12a}, at each occurrence, is independently selected from
H, OH, Cl, F, Br, I, CN, NO₂, NR¹⁵R¹⁶, -C(=O)NR¹⁵R¹⁶, CF₃, acetyl, SCH₃,
S(-O)CH₃, S(=O)₂CH₃,
C₁-C₆ alkyl, C₁-C₄ alkoxy, C₁-C₄ haloalkyl,
C₁-C₄ haloalkoxy, or C₁-C₄ haloalkyl-S-;

R^{12b}, at each occurrence, is independently selected from
H, OH, Cl, F, Br, I, CN, NO₂, NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(=O)CH₃, S(-O)₂CH₃,
C₁-C₆ alkyl, C₁-C₄ alkoxy, C₁-C₄ haloalkyl,
C₁-C₄ haloalkoxy, and C₁-C₄ haloalkyl-S-;

R¹³, at each occurrence, is independently selected from
H, OH, C₁-C₆ alkyl, C₁-C₄ alkoxy, Cl, F, Br, I, CN, NO₂, NR¹⁵R¹⁶, and CF₃;

R¹⁴ is H, phenyl, benzyl, C₁-C₆ alkyl, C₂-C₆ alkoxyalkyl, or C₃-C₆ cycloalkyl;

R^{14a} is H, phenyl, benzyl, or C₁-C₄ alkyl;

R¹⁵, at each occurrence, is independently selected from H, C₁-C₆ alkyl, benzyl, phenethyl, (C₁-C₆ alkyl) C(-O), and (C₁-C₆ alkyl)-S(=O)₂-;

R¹⁶, at each occurrence, is independently selected from

U.S. Appl. No. 09/505,788
 Response to Office Action Mailed 12/12/02
Page 12 of 93

H, OH, C₁-C₆ alkyl, benzyl, phenethyl,
 (C₁-C₆ alkyl)-C(=O)-, and (C₁-C₆ alkyl) S(=O)₂-;

R¹⁷ is H, C₁-C₆ alkyl, C₂-C₆ alkoxyalkyl,
 aryl substituted by 0-4 R^{17a}, or
 -CH₂-aryl substituted by 0-4 R^{17a};

R^{17a} is H, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, butoxy, -OH, F, Cl, Br, I,
 CF₃, OCF₃, SCH₃, S(O)CH₃, SO₂CH₃, -NH₂, -N(CH₃)₂, or C₁-C₄ haloalkyl;

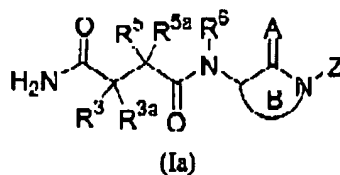
R¹⁸, at each occurrence, is independently selected from
 H, C₁-C₆ alkyl, phenyl, benzyl, phenethyl,
 (C₁-C₆ alkyl)-C(=O)-, and (C₁-C₆ alkyl)-S(=O)₂-; and

R¹⁹, at each occurrence, is independently selected from
 H, OH, C₁-C₆ alkyl, phenyl, benzyl, phenethyl,
 (C₁-C₆ alkyl)-C(=O)-, and (C₁-C₆ alkyl)-S(=O)₂-;

provided, when R¹³ is H,
 then Z is H;

C₄-C₈ alkyl substituted with 1-3 R¹²;
 C₂-C₄ alkenyl substituted with 1-3 R¹²;
 C₂-C₄ alkynyl substituted with 1-3 R¹²;
 C₁-C₈ alkyl substituted with 0-3 R^{12a};
 C₂-C₄ alkenyl substituted with 0-3 R^{12a}; or
 C₂-C₄ alkynyl substituted with 0-3 R^{12a}.

2. (PREVIOUSLY AMENDED) A compound, according to Claim 1, of Formula (Ia):



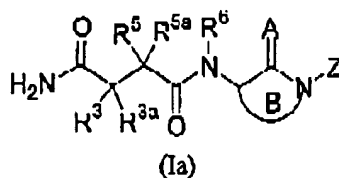
U.S. Appl. No. 09/505,788
 Response to Office Action Mailed 12/12/02
Page 13 of 93

or a pharmaceutically acceptable salt thereof,
 wherein:

Z is H;

C₁-C₈ alkyl substituted with 0-3 R^{12a},
 C₂-C₄ alkenyl substituted with 0-3 R^{12a}, or
 C₂-C₄ alkynyl substituted with 0-3 R^{12a}.

3. (PREVIOUSLY AMENDED) A compound according to Claim 2 of Formula (Ia)



or a pharmaceutically acceptable salt thereof,
 wherein:

R³ is (CR⁷R^{7a})_n-R⁴,
 -(CR⁷R^{7a})_n-S-(CR⁷R^{7a})_m-R⁴,
 -(CR⁷R^{7a})_n-O-(CR⁷R^{7a})_m-R⁴, or
 -(CR⁷R^{7a})_n-N(R^{7b})-(CR⁷R^{7a})_m-R⁴;

n is 0, 1, or 2;

m is 0, 1, or 2;

R^{3a} is H, OH, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, butoxy, allyl, or
 3-buten 1 yl;

R⁴ is H, OH, OR^{14a},
 C₁-C₆ alkyl substituted with 0-3 R^{4a},
 C₂-C₆ alkenyl substituted with 0-3 R^{4a},

U.S. Appl. No. 09/505,788
Response to Office Action Mailed 12/12/02
Page 14 of 93

C₂-C₆ alkynyl substituted with 0-3 R^{4a},
C₃-C₁₀ carbocycle substituted with 0-3 R^{4b},
C₆-C₁₀ aryl substituted with 0-3 R^{4b}, or
5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen,
oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with
0-3 R^{4b};

R^{4a}, at each occurrence, is independently selected from H, F, Cl, Br, I, CF₃,
C₃-C₁₀ carbocycle substituted with 0-3 R^{4b},
C₆-C₁₀ aryl substituted with 0-3 R^{4b}, or
5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen,
oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with
0-3 R^{4b};

R^{4b}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO₂,
NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(=O)CH₃, S(=O)₂CH₃, C₁-C₆ alkyl, C₁-C₄ alkoxy,
C₁-C₄ haloalkyl, and C₁-C₄ haloalkoxy;

R⁵ is H, OR¹⁴,
C₁-C₆ alkyl substituted with 0-3 R^{5b},
C₁-C₆ alkoxy substituted with 0-3 R^{5b},
C₂-C₆ alkenyl substituted with 0-3 R^{5b},
C₂-C₆ alkynyl substituted with 0-3 R^{5b},
C₃-C₁₀ carbocycle substituted with 0-3 R^{5c},
C₆-C₁₀ aryl substituted with 0-3 R^{5c}; or
5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen,
oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with
0-3 R^{5c};

R^{5a} is H or C₁-C₄ alkyl;

R^{5b}, at each occurrence, is independently selected from:
H, C₁-C₆ alkyl, CF₃, OR¹⁴, Cl, F, Br, I, =O, CN, NO₂, NR¹⁵R¹⁶;

U.S. Appl. No. 09/505,788
 Response to Office Action Mailed 12/12/02
 Page 15 of 93

C₃-C₁₀ carbocycle substituted with 0-3 R^{5c};
 C₆-C₁₀ aryl substituted with 0-3 R^{5c}; or
 5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen,
 oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with
 0-3 R^{5c};

R^{5c}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO₂,
 NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(=O)CH₃, S(-O)₂CH₃, C₁-C₆ alkyl, C₁-C₄ alkoxy,
 C₁-C₄ haloalkyl, and C₁-C₄ haloalkoxy;

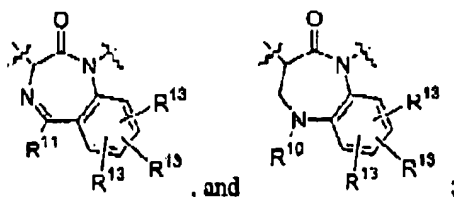
R⁶ is H, methyl, or ethyl;

R⁷, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO₂, CF₃,
 phenyl and C₁-C₄ alkyl;

R^{7a}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO₂, CF₃, and
 C₁-C₄ alkyl;

R^{7b} is independently selected from H, methyl, ethyl, propyl, and butyl;

Ring B is selected from



R¹⁰ is H, C(=O)R¹⁷, C(-O)OR¹⁷, C(-O)NR¹⁸R¹⁹,

S(-O)₂NR¹⁸R¹⁹, S(=O)₂R¹⁷;

C₁-C₆ alkyl optionally substituted with 0-2 R^{10a};

U.S. Appl. No. 09/505,788
Response to Office Action Mailed 12/12/02
Page 16 of 93

C₆-C₁₀ aryl substituted with 0-4 R^{10b};

C₃-C₁₀ carbocycle substituted with 0-3 R^{10b}; or

5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{10b};

R^{10a}, at each occurrence, is independently selected from H, C₁-C₆ alkyl, OR¹⁴, Cl, F, Br, I, -O-, CN, NO₂, NR¹⁵R¹⁶, CF₃, or phenyl substituted with 0-4 R^{10b};

R^{10b}, at each occurrence, is independently selected from H, OH, C₁-C₆ alkyl, C₁-C₄ alkoxy, Cl, F, Br, I, CN, NO₂, NR¹⁵R¹⁶, or CF₃;

R¹¹, at each occurrence, is independently selected from H, C₁-C₄ alkoxy, Cl, F, Br, I, CN, NO₂, NR¹⁸R¹⁹, C(=O)R¹⁷, C(=O)OR¹⁷, C(=O)NR¹⁸R¹⁹, S(-O)₂NR¹⁸R¹⁹, CF₃;

C₁-C₆ alkyl optionally substituted with 0-3 R^{11a};

C₆-C₁₀ aryl substituted with 0-3 R^{11b};

C₃-C₁₀ carbocycle substituted with 0-3 R^{11b}; or

5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{11b};

R^{11a}, at each occurrence, is independently selected from H, C₁-C₆ alkyl, OR¹⁴, Cl, F, Br, I, -O-, CN, NO₂, NR¹⁵R¹⁶, CF₃, or phenyl substituted with 0-3 R^{11b};

R^{11b}, at each occurrence, is independently selected from

H, OH, Cl, F, Br, I, CN, NO₂, NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(=O)CH₃, S(=O)₂CH₃,

C₁-C₆ alkyl, C₁-C₄ alkoxy, C₁-C₄ haloalkyl, and C₁-C₄ haloalkoxy;

Z is H;

C₁-C₆ alkyl substituted with 0-3 R^{12a};

C₂-C₄ alkenyl substituted with 0-3 R^{12a}; or

C₂-C₄ alkynyl substituted with 0-3 R^{12a};

U.S. Appl. No. 09/505,788
Response to Office Action Mailed 12/12/02
Page 17 of 93

R^{12a}, at each occurrence, is independently selected from

H, OH, Cl, F, Br, I, CN, NO₂, NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(=O)CH₃, S(-O)₂CH₃,
C₁-C₆ alkyl, C₁-C₄ alkoxy, C₁-C₄ haloalkyl, and C₁-C₄ haloalkoxy;

R¹³, at each occurrence, is independently selected from

H, OH, C₁-C₆ alkyl, C₁-C₄ alkoxy, Cl, F, Br, I, CN, NO₂, NR¹⁵R¹⁶, and CF₃;

R¹⁴ is H, phenyl, benzyl, C₁-C₆ alkyl, or C₂-C₆ alkoxyalkyl;

R^{14a} is H, phenyl, benzyl, methyl, ethyl, propyl, or butyl;

R¹⁵, at each occurrence, is independently selected from H, C₁-C₆ alkyl, benzyl, phenethyl, (C₁-C₆ alkyl)-C(=O)-, and (C₁-C₆ alkyl)-S(=O)₂-;

R¹⁶, at each occurrence, is independently selected from

H, OH, C₁-C₆ alkyl, benzyl, phenethyl,
(C₁-C₆ alkyl)-C(=O)-, and (C₁-C₆ alkyl)-S(=O)₂-;

R¹⁷ is H, C₁-C₆ alkyl, C₂-C₆ alkoxyalkyl,

aryl substituted by 0-4 R^{17a}, or
-CH₂-aryl substituted by 0-4 R^{17a};

R^{17a} is H, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, butoxy, -OH, F, Cl, Br, I,
CF₃, OCF₃, SCH₃, S(O)CH₃, SO₂CH₃, -NH₂, N(CH₃)₂, or C₁-C₄ haloalkyl;

R¹⁸, at each occurrence, is independently selected from

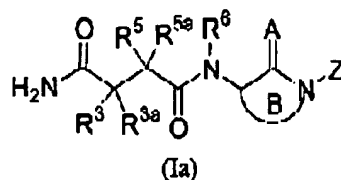
H, C₁-C₆ alkyl, phenyl, benzyl, phenethyl,
(C₁-C₆ alkyl)-C(=O)-, and (C₁-C₆ alkyl)-S(=O)₂-; and

R¹⁹, at each occurrence, is independently selected from

H, OH, C₁-C₆ alkyl, phenyl, benzyl, phenethyl,
(C₁-C₆ alkyl)-C(=O)-, and (C₁-C₆ alkyl)-S(=O)₂-.

U.S. Appl. No. 09/505,788
 Response to Office Action Mailed 12/12/02
Page 18 of 93

4. (PREVIOUSLY AMENDED) A compound according to Claim 3 of Formula (Ia)



or a pharmaceutically acceptable salt thereof,
 wherein:

R^3 is $-(CHR^7)_n-R^4$,

n is 0 or 1;

R^{3a} is H, OH, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, butoxy, allyl, or 3-buten-1-yl;

R^4 is H, OH, OR^{4a},

C₁-C₄ alkyl substituted with 0-2 R^{4a},

C₂-C₄ alkenyl substituted with 0-2 R^{4a},

C₂-C₄ alkynyl substituted with 0-1 R^{4a},

C₃-C₆ carbocycle substituted with 0-3 R^{4b},

C₆-C₁₀ aryl substituted with 0-3 R^{4b}, or

5 to 6 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-3 R^{4b};

R^{4a}, at each occurrence, is independently selected from H, F, Cl, Br, I, CF₃,

C₃-C₆ carbocycle substituted with 0-3 R^{4b},

phenyl substituted with 0-3 R^{4b}, or

U.S. Appl. No. 09/505,788
Response to Office Action Mailed 12/12/02
Page 19 of 93

5 to 6 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-3 R^{4b};

R^{4b}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO₂, NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(-O)CH₃, S(=O)₂CH₃, C₁-C₄ alkyl, C₁-C₃ alkoxy, C₁-C₂ haloalkyl, and C₁-C₂ haloalkoxy;

R⁵ is H, OR¹⁴;
C₁-C₄ alkyl substituted with 0-3 R^{5b};
C₂-C₄ alkenyl substituted with 0-3 R^{5b};
C₂-C₄ alkynyl substituted with 0-3 R^{5b};

R^{5a} is H, methyl, ethyl, propyl, or butyl;

R^{5b}, at each occurrence, is independently selected from:
H, methyl, ethyl, propyl, butyl, CF₃, OR¹⁴, Cl, F, Br, I, -O;
C₃-C₆ carbocycle substituted with 0-3 R^{5c};
phenyl substituted with 0-3 R^{5c}; or
5 to 6 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-3 R^{5c};

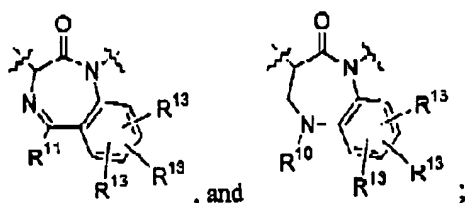
R^{5c}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO₂, NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(=O)CH₃, S(-O)₂CH₃, C₁-C₄ alkyl, C₁-C₃ alkoxy, C₁-C₂ haloalkyl, and C₁-C₂ haloalkoxy;

R⁶ is H;

R⁷, at each occurrence, is independently selected from H, F, CF₃, methyl, and ethyl;

Ring B is selected from

U.S. Appl. No. 09/505,788
 Response to Office Action Mailed 12/12/02
Page 20 of 93



R^{10} is H, $C(=O)R^{17}$, $C(=O)OR^{17}$;

C_1 - C_4 alkyl optionally substituted with 0-1 R^{10a} ;

phenyl substituted with 0-4 R^{10b} ;

C_3 - C_6 carbocycle substituted with 0-3 R^{10b} ; or

5 to 6 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-3 R^{10b} ;

R^{10a} is selected from H, C_1 - C_4 alkyl, OR^{14} , Cl, F, Br, I, =O, CN, NO_2 , $NR^{15}R^{16}$, CF_3 , or phenyl substituted with 0-4 R^{10b} ;

R^{10b} , at each occurrence, is independently selected from H, OH, C_1 - C_4 alkyl, C_1 - C_3 alkoxy, Cl, F, Br, I, CN, NO_2 , $NR^{15}R^{16}$, or CF_3 ;

R^{11} is selected from

H, C_1 - C_4 alkoxy, Cl, F, $NR^{18}R^{19}$, $C(=O)R^{17}$, $C(=O)OR^{17}$, CF_3 ;

C_1 - C_6 alkyl optionally substituted with 0-3 R^{11a} ;

C_6 - C_{10} aryl substituted with 0-3 R^{11b} ;

C_3 - C_6 carbocycle substituted with 0-3 R^{11b} ; or

5 to 6 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-3 R^{11b} ;

R^{11a} , at each occurrence, is independently selected from H, C_1 - C_4 alkyl, OR^{14} , F, =O, $NR^{15}R^{16}$, CF_3 , or phenyl substituted with 0-3 R^{11b} ;

U.S. Appl. No. 09/505,788
Response to Office Action Mailed 12/12/02
Page 21 of 93

R^{11b}, at each occurrence, is independently selected from H, OH, Cl, F, NR¹⁵R¹⁶, CF₃, C₁-C₄ alkyl, C₁-C₃ alkoxy, C₁-C₂ haloalkyl, and C₁-C₂ haloalkoxy;

Z is H;

C₁-C₄ alkyl substituted with 0-3 R^{12a};
C₂-C₄ alkenyl substituted with 0-3 R^{12a}; or
C₂-C₄ alkynyl substituted with 0-3 R^{12a};

R^{12a}, at each occurrence, is independently selected from
H, OH, Cl, F, NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(=O)CH₃, S(-O)₂CH₃, C₁-C₄ alkyl,
C₁-C₃ alkoxy, C₁-C₂ haloalkyl, and C₁-C₂ haloalkoxy;

R¹³, at each occurrence, is independently selected from
H, OH, C₁-C₆ alkyl, C₁-C₄ alkoxy, Cl, F, Br, I, CN, NO₂, NR¹⁵R¹⁶, and CF₃;

R¹⁴ is H, phenyl, benzyl, C₁-C₄ alkyl, or C₂-C₄ alkoxyalkyl;

R¹⁵, at each occurrence, is independently selected from H, C₁-C₄ alkyl, benzyl, phenethyl, (C₁-C₄ alkyl)-C(=O)-, and (C₁-C₄ alkyl)-S(=O)₂-;

R¹⁶, at each occurrence, is independently selected from
H, OH, C₁-C₄ alkyl, benzyl, phenethyl,
(C₁-C₄ alkyl)-C(=O)-, and (C₁-C₄ alkyl)-S(=O)₂-;

R¹⁷ is H, methyl, ethyl, propyl, butyl, methoxymethyl, ethoxymethyl, methoxyethyl,
ethoxyethyl,
phenyl substituted by 0-3 R^{17a}, or
-CH₂-phenyl substituted by 0-3 R^{17a};

R^{17a} is H, methyl, methoxy, -OH, F, Cl, CF₃, or OCF₃;

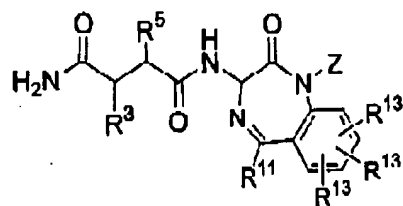
R¹⁸, at each occurrence, is independently selected from
H, methyl, ethyl, propyl, butyl, phenyl, benzyl, and phenethyl; and

U.S. Appl. No. 09/505,788
 Response to Office Action Mailed 12/12/02
Page 22 of 93

R^{19} , at each occurrence, is independently selected from
 H, methyl, and ethyl.

5. (Canceled)

6. (Previously Amended) A compound according to Claim 4 of Formula (Ic):



(Ic)

or a pharmaceutically acceptable salt thereof
 wherein

R^3 is R^4 .

R^4 is C₁-C₄ alkyl substituted with 0-1 R^{4a} ,
 C₂-C₄ alkenyl substituted with 0-1 R^{4a} , or
 C₂-C₄ alkynyl substituted with 0-1 R^{4a} ;

R^{4a} is selected from

H, F, CF₃,

C₃-C₆ carbocyclic substituted with 0-3 R^{4b} ,

phenyl substituted with 0-3 R^{4b} , or

5 to 6 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen,
 oxygen, and sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-
 3 R^{4b} ; wherein said 5 to 6 membered heterocycle is selected from pyridinyl,

U.S. Appl. No. 09/505,788
 Response to Office Action Mailed 12/12/02
Page 23 of 93

pyrimidinyl, triazinyl, furanyl, thienyl, thiazolyl, pyrrolyl, piperazinyl, piperidinyl, pyrazolyl, imidazolyl, oxazolyl, isoxazolyl, and tetrazolyl;

R^{4b}, at each occurrence, is independently selected from H, OH, Cl, F, NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(=O)CH₃, S(=O)₂CH₃, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, C₁-C₂ haloalkyl, and C₁-C₂ haloalkoxy;

R⁵ is C₁-C₄ alkyl substituted with 0-1 R^{5b};
 C₂-C₄ alkenyl substituted with 0-1 R^{5b};
 C₂-C₄ alkynyl substituted with 0-1 R^{5b};

R^{5b} is selected from:

H, methyl, ethyl, propyl, butyl, CF₃, OR¹⁴, -O;
 C₃-C₆ carbocycle substituted with 0-2 R^{5c};
 phenyl substituted with 0-3 R^{5c}; or
 5 to 6 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-3 R^{5c}; wherein said 5 to 6 membered heterocycle is selected from pyridinyl, pyrimidinyl, triazinyl, furanyl, thienyl, thiazolyl, pyrrolyl, piperazinyl, piperidinyl, pyrazolyl, imidazolyl, oxazolyl, isoxazolyl, and tetrazolyl;

R^{5c}, at each occurrence, is independently selected from H, OH, Cl, F, NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(=O)CH₃, S(=O)₂CH₃, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, C₁-C₂ haloalkyl, and C₁-C₂ haloalkoxy;

R¹¹ is selected from

H, NR¹⁸R¹⁹, CF₃;
 C₁-C₄ alkyl optionally substituted with 0-1 R^{11a};
 phenyl substituted with 0-3 R^{11b};
 C₃-C₆ carbocycle substituted with 0-3 R^{11b}; and
 5 to 6 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-3 R^{11b}; wherein said 5 to 6 membered heterocycle is selected from pyridinyl,

U.S. Appl. No. 09/505,788
Response to Office Action Mailed 12/12/02
Page 24 of 93

pyrimidinyl, triazinyl, furanyl, thienyl, thiazolyl, pyrrolyl, piperazinyl, piperidinyl,
pyrazolyl, imidazolyl, oxazolyl, isoxazolyl, and tetrazolyl;

R^{11a} is selected from H, C₁-C₄ alkyl, OR¹⁴, F, =O, NR¹⁵R¹⁶, CF₃, or phenyl substituted
with 0-3 R^{11b};

R^{11b}, at each occurrence, is independently selected from H, OH, Cl, F, NR¹⁵R¹⁶, CF₃, methyl,
ethyl, propyl, butyl, methoxy, ethoxy, propoxy, C₁-C₂ haloalkyl, and C₁-C₂ haloalkoxy;

Z is H;

C₁-C₄ alkyl substituted with 0-3 R^{12a};
C₂-C₄ alkenyl substituted with 0-3 R^{12a}; or
C₂-C₄ alkynyl substituted with 0-3 R^{12a};

R^{12a}, at each occurrence, is independently selected from
H, OH, Cl, F, NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(=O)CH₃, S(=O)₂CH₃, methyl, ethyl,
propyl, butyl, methoxy, ethoxy, propoxy, C₁-C₂ haloalkyl, and C₁-C₂ haloalkoxy;

R¹³, at each occurrence, is independently selected from
H, OH, methyl, ethyl, propyl, butyl, methoxy, ethoxy, Cl, F, Br, CN, NR¹⁵R¹⁶, and CF₃;

R¹⁴ is H, phenyl, benzyl, methyl, ethyl, propyl, or butyl;

R¹⁵, at each occurrence, is independently selected from H, methyl, ethyl, propyl, and butyl;

R¹⁶, at each occurrence, is independently selected from
H, OH, methyl, ethyl, propyl, butyl, benzyl, phenethyl, methyl-C(=O)-, ethyl-C(=O)-,
methyl-S(=O)₂-, and ethyl-S(=O)₂-;

R¹⁸, at each occurrence, is independently selected from
H, methyl, ethyl, propyl, butyl, phenyl, benzyl, and phenethyl; and

R¹⁹, at each occurrence, is independently selected from

U.S. Appl. No. 09/505,788
 Response to Office Action Mailed 12/12/02
Page 25 of 93

II, methyl, and ethyl.

7. - 9 (Canceled)

10. (Currently Amended) A compound, according to Claim 6, wherein:

R³ is -CH₃, -CH₂CH₃, -CH₂CH₂CH₃, -CH₂CH₂CH₂CH₃,
 -CH(CH₃)₂, -CH(CH₃)CH₂CH₃, -CH₂CH(CH₃)₂,
 -CH₂CF₃, -CH₂CH₂CF₃, -CH₂CH₂CH₂CF₃,
 -CH=CH₂, -CH₂CH=CH₂, -CH₂C(CH₃)=CH₂,
 -CH₂CH₂CH=CH₂,
 cis-CH₂CH=CH(CH₃),
 trans-CH₂CH=CH(CH₃),
~~-C≡CH, -CH₂C≡CH, -CH₂C≡C(CH₃), -CH₂C≡C(CH₃),~~
 cyclopropyl-CH₂-, cyclobutyl-CH₂-, cyclopentyl-CH₂-, cyclohexyl-CH₂-, cyclopropyl
 CH₂CH₂-,
 cyclobutyl CH₂CH₂-, cyclopentyl-CH₂CH₂-,
 cyclohexyl CH₂CH₂-, phenyl-CH₂-,
 (2-F-phenyl)CH₂-, (3-F-phenyl)CH₂-, (4-F-phenyl)CH₂-,
 (2-Cl-phenyl)CH₂-, (3-Cl-phenyl)CH₂-, (4-Cl-phenyl)CH₂-,
 (2,3-diF-phenyl)CH₂-, (2,4-diF-phenyl)CH₂-,
 (2,5-diF-phenyl)CH₂-, (2,6-diF-phenyl)CH₂-,
 (3,4-diF-phenyl)CH₂-, (3,5-diF-phenyl)CH₂-,
 (2,3-diCl-phenyl)CH₂-, (2,4-diCl-phenyl)CH₂-,
 (2,5-diCl-phenyl)CH₂-, (2,6-diCl-phenyl)CH₂-,
 (3,4-diCl-phenyl)CH₂-, (3,5-diCl-phenyl)CH₂-,
 (3-F-4-Cl-phenyl)CH₂-, (3-F-5-Cl-phenyl)CH₂-,
 (3-Cl-4-F-phenyl)CH₂-, phenyl-CH₂CH₂CH₂-,
 (2-F-phenyl)CH₂CH₂CH₂-, (3-F-phenyl)CH₂CH₂CH₂-,
 (4-F-phenyl)CH₂CH₂CH₂-, (2-Cl-phenyl)CH₂CH₂CH₂-,
 (3-Cl-phenyl)CH₂CH₂CH₂-, (4-Cl-phenyl)CH₂CH₂CH₂-.

U.S. Appl. No. 09/505,788
 Response to Office Action Mailed 12/12/02
Page 26 of 93

(2,3-diF-phenyl)CH₂CH₂-, (2,4-diF-phenyl)CH₂CH₂-,
 (2,5-diF-phenyl)CH₂CH₂-, (2,6-diF-phenyl)CH₂CH₂-,
 (3,4-diF-phenyl)CH₂CH₂-, (3,5-diF-phenyl)CH₂CH₂-,
 (2,3-diCl-phenyl)CH₂CH₂-, (2,4-diCl-phenyl)CH₂CH₂-,
 (2,5-diCl-phenyl)CH₂CH₂-, (2,6-diCl-phenyl)CH₂CH₂-,
 (3,4-diCl-phenyl)CH₂CH₂-, (3,5-diCl-phenyl)CH₂CH₂-,
 (3-F-4-Cl-phenyl)CH₂CH₂-, or (3-F-5-Cl-phenyl)CH₂CH₂-,

R⁵ is -CH₃, -CH₂CH₂CH₃, -CH(CH₃)₂, -CH₂CH₂CH₂CH₃,
 -CH(CH₃)CH₂CH₃, -CH₂CH(CH₃)₂, -CH₂C(CH₃)₃,
 -CH₂CH₂CH₂CH₂CH₃, -CH(CH₃)CH₂CH₂CH₃, -CH₂CH(CH₃)CH₂CH₃,
 -CH₂CH₂CH(CH₃)₂, -CH(CH₂CH₃)₂, -CH₂CF₃, -CH₂CH₂CF₃,
 -CH₂CH₂CH₂CF₃, -CH₂CH₂CH₂CH₂CF₃, -CH=CH₂, -CH₂CH=CH₂,
 -CH=CHCH₃, cis-CH₂CH=CH(CH₃), trans-CH₂CH=CH(CH₃),
 trans-CH₂CH=CH(C₆H₅), -CH₂CH=C(CH₃)₂, cis-CH₂CH-CHCH₂CH₃,
 trans-CH₂CH=CHCH₂CH₃, cis-CH₂CH₂CH=CH(CH₃),
 (trans-CH₂CH₂CH=CH(CH₃), trans-CH₂CH-CHCH₂(C₆H₅),
~~-C≡CH, -CH₂C≡CH, -CH₂C≡C(CH₃), -CH₂C≡C(C₆H₅),~~
~~-CH₂CH₂C≡CH, -CH₂CH₂C≡C(CH₃), -CH₂CH₂C≡C(C₆H₅),~~
~~-C≡CH, -CH₂C≡CH, -CH₂C≡C(CH₃), -CH₂C≡C(C₆H₅),~~
~~-CH₂CH₂C≡CH, -CH₂CH₂C≡C(CH₃), -CH₂CH₂C≡C(C₆H₅),~~
 cyclopropyl-CH₂-, cyclobutyl-CH₂-, cyclopentyl-CH₂-,
 cyclohexyl-CH₂-, (2-CH₃-cyclopropyl)CH₂-,
 (3-CH₃-cyclobutyl)CH₂-,
 cyclopropyl-CH₂CH₂-, cyclobutyl-CH₂CH₂-,
 cyclopentyl-CH₂CH₂-, cyclohexyl-CH₂CH₂-,
 (2-CH₃-cyclopropyl)CH₂CH₂-, (3-CH₃-cyclobutyl)CH₂CH₂-,
 phenyl-CH₂-, (2-F-phenyl)CH₂-, (3-F-phenyl)CH₂-,
 (4-F-phenyl)CH₂-, furanyl-CH₂-, thienyl-CH₂-,
 pyridyl-CH₂-, 1-imidazolyl-CH₂-, oxazolyl-CH₂-,
 isoxazolyl-CH₂-,
 phenyl-CH₂CH₂-, (2-F-phenyl)CH₂CH₂-, (3-F-phenyl)CH₂CH₂-,
 (4-F-phenyl)CH₂CH₂-, furanyl-CH₂CH₂-, thienyl-CH₂CH₂-,
 pyridyl-CH₂CH₂-, 1-imidazolyl-CH₂CH₂-, oxazolyl-CH₂CH₂-,

U.S. Appl. No. 09/505,788
 Response to Office Action Mailed 12/12/02
 Page 27 of 93

isoxazolyl-CH₂CH₂;

Z is methyl, ethyl, i-propyl, n-propyl, n-butyl, i-butyl, s-butyl, t-butyl, or allyl;

R¹⁰ is H, methyl, ethyl, phenyl, benzyl, phenethyl,
 4-F-phenyl, (4-F-phenyl)CH₂-, (4-F-phenyl)CH₂CH₂-,
 4-Cl-phenyl, (4-Cl-phenyl)CH₂-, (4-Cl-phenyl)CH₂CH₂-,
 4-CH₃-phenyl, (4-CH₃-phenyl)CH₂-, (4-CH₃-phenyl)CH₂CH₂-,
 4-CF₃-phenyl, (4-CF₃-phenyl)CH₂-, or
 (4-CF₃-phenyl)CH₂CH₂-;

R¹¹, at each occurrence, is independently selected from
 H, [(=O)], methyl, ethyl, phenyl, benzyl, phenethyl,
 4-F-phenyl, (4-F-phenyl)CH₂-, (4-F-phenyl)CH₂CH₂-,
 3-F-phenyl, (3-F-phenyl)CH₂-, (3-F-phenyl)CH₂CH₂-,
 2-F-phenyl, (2-F-phenyl)CH₂-, (2-F-phenyl)CH₂CH₂-,
 4-Cl-phenyl, (4-Cl-phenyl)CH₂-, (4-Cl-phenyl)CH₂CH₂-,
 3-Cl-phenyl, (3-Cl-phenyl)CH₂-, (3-Cl-phenyl)CH₂CH₂-,
 4-CH₃-phenyl, (4-CH₃-phenyl)CH₂-, (4-CH₃-phenyl)CH₂CH₂-,
 3-CH₃-phenyl, (3-CH₃-phenyl)CH₂-, (3-CH₃-phenyl)CH₂CH₂-,
 4-CF₃-phenyl, (4-CF₃-phenyl)CH₂-, (4-CF₃-phenyl)CH₂CH₂-,
 pyrid-2-yl, pyrid-3-yl, or pyrid-4-yl, and

R¹³, at each occurrence, is independently selected from
 H, F, Cl, OH, -CH₃, -CH₂CH₃, -OCH₃, or -CF₃.

11. (PREVIOUSLY AMENDED) A compound according to Claim 2 selected from:

(2R,3S) N1-[1,3-dihydro-1-methyl-2-oxo-5-phenyl-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-allyl-butanediamide;

(2R,3S) N1-[1,3-dihydro-1-methyl-2-oxo-5-phenyl-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-propyl-butanediamide;

U.S. Appl. No. 09/505,788
Response to Office Action Mailed 12/12/02
Page 28 of 93

(2R,3S) N1-[(3S)-1,3-dihydro-1-methyl-2-oxo-5-phenyl-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-allyl-butanediamide;

(2R,3S) N1-[(3R)-1,3-dihydro-1-methyl-2-oxo-5-phenyl-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-allyl-butanediamide;

(2R,3S) N1-[(3R)-1,3-dihydro-1-methyl-2-oxo-5-phenyl-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-propyl-butanediamide;

(2R,3S) N1-[(3S)-1,3-dihydro-1-methyl-2-oxo-5-phenyl-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-propyl butanediamide;

(2R,3S) N1-[1,3-dihydro-1-methyl-2-oxo-5-phenyl-2H-1,4-benzodiazepin-3-yl]-2-methyl-3-allyl-butanediamide;

(2R,3S) N1-[(3S)-1,3-dihydro-1-methyl-2-oxo-5-phenyl-2H-1,4-benzodiazepin-3-yl]-2-methyl-3-allyl-butanediamide;

(2R,3S) N1-[(3S)-1,3-dihydro-1-methyl-2-oxo-5-phenyl-2H-1,4-benzodiazepin-3-yl]-2-methyl-3-propyl-butanediamide;

(2R) N1-[1,3-dihydro-1-methyl-2-oxo-5-phenyl-2H-1,4-benzodiazepin-3-yl]-2-methyl-butanediamide;

(2R,3S) N1-[1,3-dihydro-2-oxo-5-phenyl-2H-1,4-benzodiazepin-3-yl]-2 (2-methylpropyl)-3-allyl-butanediamide;

(2R,3S) N1-[1,3-dihydro-1-methyl-2-oxo-5-phenyl-7-chloro-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-allyl-butanediamide;

(2R,3S) N1-[(3S)-1,3-dihydro-1-methyl-2-oxo-5-phenyl-7-chloro-2H-1,4-benzodiazepin-3-yl] 2 (2-methylpropyl)-3-allyl-butanediamide;

U.S. Appl. No. 09/505,788
 Response to Office Action Mailed 12/12/02
Page 29 of 93

(2R,3S) N1-[(3R)-1,3-dihydro-1-methyl-2-oxo-5-phenyl-7-chloro-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-allyl-butanediamide;

(2R,3S) N1-[1,3-dihydro-1-methyl-2-oxo-5-(2-fluorophenyl)-7-chloro-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-allyl-butanediamide;

(2R,3S) N1-[(3S)-1,3-dihydro-1-methyl-2-oxo-5-(2-fluorophenyl)-7-chloro-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-allyl-butanediamide;

(2R,3S) N1-[(3R)-1,3-dihydro-1-methyl-2-oxo-5-(2-fluorophenyl)-7-chloro-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-allyl-butanediamide;

(2S,3S) N1-[1,3-dihydro-1-methyl-2-oxo-5-phenyl-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-allyl-butanediamide;

(2R,3S) N1-[(3S)-1,3-dihydro-1-methyl-2-oxo-5-phenyl-7-chloro-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-propyl-butanediamide;

(2R,3S) N1-[(3S)-1,3-dihydro-1-methyl-2-oxo-5-(2-fluorophenyl)-7-chloro-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-propyl-butanediamide;

(2R,3S) N1-[1,3-dihydro-1-methyl-2-oxo-5-(4-fluorophenyl)-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-allyl-butanediamide;

(2R,3S) N1-[(3S)-1,3-dihydro-1-methyl-2-oxo-5-(4-fluorophenyl)-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-allyl-butanediamide;

(2R,3S) N1-[(3R)-1,3-dihydro-1-methyl-2-oxo-5-(4-fluorophenyl)-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-allyl-butanediamide;

(2R,3S) N1-[1,3-dihydro-1-methyl-2-oxo-5-(pyrid-2-yl)-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-allyl-butanediamide;

U.S. Appl. No. 09/505,788
Response to Office Action Mailed 12/12/02
Page 30 of 93

(2R,3S) N1-[1,3-dihydro-1-methyl-2-oxo-5-(N-morpholino)-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-allyl-butanediamide;

(2R,3S) N1-[1,3-dihydro-1-methyl-2-oxo-5-(dimethylamino)-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-allyl-butanediamide;

(2R,3S) N1-[1,3-dihydro-1-methyl-2-oxo-5-(N-methyl-N-phenylamino)-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-allyl-butanediamide;

(2R,3S) N1-[1,3-dihydro-1-methyl-2-oxo-5-(N-piperidinyl)-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-allyl-butanediamide;

(2R,3S) N1-[1,3-dihydro-1-methyl-2-oxo-5-(N-homopiperidinyl)-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-allyl-butanediamide;

(2R,3S) N1-[1,3-dihydro-1-methyl-2-oxo-5-(3-methoxyphenyl)-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-allyl-butanediamide;

(2R,3S) N1-[1,3-dihydro-1-methyl-2-oxo-5-(pyrid-4-yl)-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-allyl-butanediamide;

(2R,3S) N1-[1,3-dihydro-1-methyl-2-oxo-5-phenyl-7-methoxy-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-allyl-butanediamide;

(2R,3S) N1-[1,3-dihydro-1-methyl-2-oxo-5-(pyrid-3-yl)-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-allyl-butanediamide;

(2R,3S) N1-[1,3-dihydro-1-methyl-2-oxo-5-phenyl-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-(cyclopropylmethyl)-butanediamide;

(2R,3S) N1-[1,3-dihydro-1-methyl-2-oxo-5-(3-fluorophenyl)-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-allyl-butanediamide;

U.S. Appl. No. 09/505,788
 Response to Office Action Mailed 12/12/02
Page 31 of 93

(2R,3S) N1-[(3S)-1,3-dihydro-1-methyl-2-oxo-5-(3-fluorophenyl)-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-allyl-butanediamide;

(2R,3S) N1-[(3R)-1,3-dihydro-1-methyl-2-oxo-5-(3-fluorophenyl)-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-allyl-butanediamide;

(2R,3S) N1-[(3S)-1,3-dihydro-1-methyl-2-oxo-5-phenyl-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-(3-buten-1-yl)-butanediamide;

(2R,3S) N1-[(3S)-1,3-dihydro-1-methyl-2-oxo-5-phenyl-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-(cyclopentylethyl)-butanediamide;

(2R,3S) N1-[(3S)-1,3-dihydro-1-methyl-2-oxo-5-(4-trifluoromethylphenyl)-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-(3-buten-1-yl)-butanediamide;

(2R,3S) N1-[(3R)-1,3-dihydro-1-methyl-2-oxo-5-(4-trifluoromethylphenyl)-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-(3-buten-1-yl)-butanediamide;

(2R,3S) N1-[(3S)-1,3-dihydro-1-methyl-2-oxo-5-(4-trifluoromethylphenyl)-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-allyl-butanediamide;

(2R,3S) N1-[(3S)-1,3-dihydro-1-methyl-2-oxo-5-(4-trifluoromethylphenyl)-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-allyl-butanediamide;

(2R,3S) N1-[(3R)-1,3-dihydro-1-methyl-2-oxo-5-(4-trifluoromethylphenyl)-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-allyl-butanediamide;

(2R,3S) N1-[(3S)-1,3-dihydro-1-methyl-2-oxo-5-(4-trifluoromethylphenyl)-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-n-butyl-butanediamide;

(2R,3S) N1-[(3S)-1,3-dihydro-1-methyl-2-oxo-5-(4-trifluoromethylphenyl)-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-propyl-butanediamide;

U.S. Appl. No. 09/505,788
 Response to Office Action Mailed 12/12/02
Page 32 of 93

(2R,3S) N1-[(3S)-1,3-dihydro-1-methyl-2-oxo-5-(4-chlorophenyl)-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-(3-buten-1-yl)-butanediamide;

(2R,3S) N1-[(3S)-1,3-dihydro-1-methyl-2-oxo-5-(4-chlorophenyl)-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-n-butyl-butanediamide;

(2R,3S) N1-[(3S)-1,3-dihydro-1-methyl-2-oxo-5-phenyl-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-allyl-N4-[benzyl]-butanediamide;

(2R,3S) N1-[1,3-dihydro-1-methyl-2-oxo-5-methyl-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-allyl-butanediamide;

(2R,3S) N1-[1,3-dihydro-1-methyl-2-oxo-5-n-butyl-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-allyl-butanediamide;

(2R,3S) N1-[1,3-dihydro-1-methyl-2-oxo-5-(2-methylpropyl)-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-allyl-butanediamide;

(2R,3S) N1-[1,3-dihydro-1-methyl-2-oxo-5-(4-chlorophenyl)-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-allyl-butanediamide;

(2R,3S) N1-[1,3-dihydro-1-ethyl-2-oxo-5-phenyl-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-allyl-butanediamide;

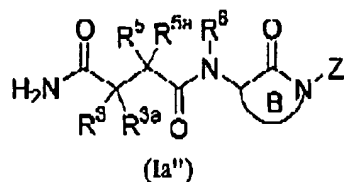
(2R,3S) N1-[1,3-dihydro-1-propyl-2-oxo-5-phenyl-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-allyl-butanediamide;

(2R,3S) N1-[1,3-dihydro-1-(isopropyl)-2-oxo-5-phenyl-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3-allyl-butanediamide; and

(2R,3S) N1-[(3S)-1,3-dihydro-1-methyl-2-oxo-5-phenyl-2H-1,4-benzodiazepin-3-yl]-2-(2-methylpropyl)-3,3-diallyl-butanediamide.

U.S. Appl. No. 09/505,788
 Response to Office Action Mailed 12/12/02
Page 33 of 93

12. (PREVIOUSLY AMENDED) A compound, according to Claim 1, of Formula (Ia''):



or a pharmaceutically acceptable salt thereof,
 wherein:

Z is C₁-C₈ alkyl substituted with 1-3 R¹²;

C₂-C₄ alkenyl substituted with 1-3 R¹²;

C₂-C₄ alkynyl substituted with 1-3 R¹²;

C₆-C₁₀ aryl substituted with 0-4 R^{12b};

C₃-C₁₀ carbocycle substituted with 0-4 R^{12b}; or

5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen,
 oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with
 0-3 R^{12b};

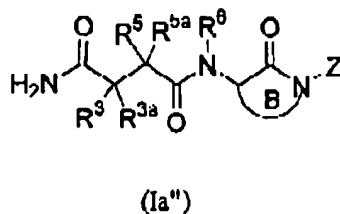
provided, when R¹³ is H,

then Z is C₄-C₈ alkyl substituted with 1-3 R¹²;

C₂-C₄ alkenyl substituted with 1-3 R¹²; or

C₂-C₄ alkynyl substituted with 1-3 R¹².

13. (PREVIOUSLY AMENDED) A compound according to Claim 12 of Formula (Ia'')



U.S. Appl. No. 09/505,788
 Response to Office Action Mailed 12/12/02
Page 34 of 93

or a pharmaceutically acceptable salt thereof,
 wherein:

R^3 is $(CR^7R^{7a})_n-R^4$,
 $-(CR^7R^{7a})_n-S-(CR^7R^{7a})_m-R^4$,
 $-(CR^7R^{7a})_n-O-(CR^7R^{7a})_m-R^4$, or
 $-(CR^7R^{7a})_n-N(R^{7b})-(CR^7R^{7a})_m-R^4$;

n is 0, 1, or 2;

m is 0, 1, or 2;

R^{3a} is H, OH, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, butoxy, allyl, or 3-buten-1-yl;

R^4 is H, OH, OR^{14a},
 C₁-C₆ alkyl substituted with 0-3 R^{4a},
 C₂-C₆ alkenyl substituted with 0-3 R^{4a},
 C₂-C₆ alkynyl substituted with 0-3 R^{4a},
 C₃-C₁₀ carbocycle substituted with 0-3 R^{4b},
 C₆-C₁₀ aryl substituted with 0-3 R^{4b}, or
 5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{4b};

R^{4a} , at each occurrence, is independently selected from H, F, Cl, Br, I, CF₃,

C₃-C₁₀ carbocycle substituted with 0-3 R^{4b},
 C₆-C₁₀ aryl substituted with 0-3 R^{4b}, or
 5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{4b};

U.S. Appl. No. 09/505,788
Response to Office Action Mailed 12/12/02
Page 35 of 93

R^{4b}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO₂, NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(=O)CH₃, S(-O)₂CH₃, C₁-C₆ alkyl, C₁-C₄ alkoxy, C₁-C₄ haloalkyl, and C₁-C₄ haloalkoxy;

R⁵ is H, OR¹⁴;

C₁-C₆ alkyl substituted with 0-3 R^{5b};

C₁-C₆ alkoxy substituted with 0-3 R^{5b};

C₂-C₆ alkenyl substituted with 0-3 R^{5b};

C₂-C₆ alkynyl substituted with 0-3 R^{5b};

C₃-C₁₀ carbocycle substituted with 0-3 R^{5c};

C₆-C₁₀ aryl substituted with 0-3 R^{5c}; or

5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{5c};

R^{5a} is H or C₁-C₄ alkyl;

R^{5b}, at each occurrence, is independently selected from:

H, C₁-C₆ alkyl, CF₃, OR¹⁴, Cl, F, Br, I, =O, CN, NO₂, NR¹⁵R¹⁶;

C₃-C₁₀ carbocycle substituted with 0-3 R^{5c};

C₆-C₁₀ aryl substituted with 0-3 R^{5c}; or

5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{5c};

R^{5c}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO₂,

NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(=O)CH₃, S(-O)₂CH₃, C₁-C₆ alkyl, C₁-C₄ alkoxy,

C₁-C₄ haloalkyl, and C₁-C₄ haloalkoxy;

R⁶ is H, methyl, or ethyl;

R⁷, at each occurrence, is independently selected from

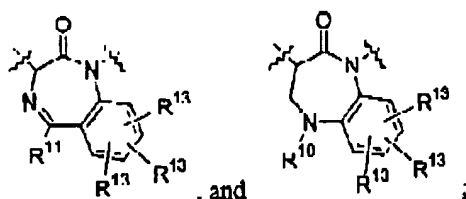
H, OH, Cl, F, Br, I, CN, NO₂, CF₃, phenyl, and C₁-C₄ alkyl;

U.S. Appl. No. 09/505,788
 Response to Office Action Mailed 12/12/02
Page 36 of 93

R^{7a}, at each occurrence, is independently selected from
 H, OH, Cl, F, Br, I, CN, NO₂, CF₃, and C₁-C₄ alkyl;

R^{7b} is independently selected from H, methyl, ethyl, propyl, and butyl;

Ring B is selected from



R¹⁰ is H, C(-O)R¹⁷, C(-O)OR¹⁷, C(-O)NR¹⁸R¹⁹,
 S(-O)₂NR¹⁸R¹⁹, S(=O)₂R¹⁷;

C₁-C₆ alkyl optionally substituted with 0-2 R^{10a};

C₆-C₁₀ aryl substituted with 0-4 R^{10b};

C₃-C₁₀ carbocycle substituted with 0-3 R^{10b}; or

5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen,
 oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with
 0-3 R^{10b};

R^{10a}, at each occurrence, is independently selected from H, C₁-C₆ alkyl, OR¹⁴, Cl, F, Br, I, =O,
 CN, NO₂, NR¹⁵R¹⁶, CF₃, or phenyl substituted with 0-4 R^{10b};

R^{10b}, at each occurrence, is independently selected from H, OH, C₁-C₆ alkyl, C₁-C₄ alkoxy,
 Cl, F, Br, I, CN, NO₂, NR¹⁵R¹⁶, or CF₃;

R¹¹, at each occurrence, is independently selected from

U.S. Appl. No. 09/505,788
 Response to Office Action Mailed 12/12/02
Page 37 of 93

H, C₁-C₄ alkoxy, Cl, F, Br, I, CN, NO₂, NR¹⁸R¹⁹, C(=O)R¹⁷, C(=O)OR¹⁷,
 C(=O)NR¹⁸R¹⁹, S(=O)₂NR¹⁸R¹⁹, CF₃;
 C₁-C₆ alkyl optionally substituted with 0-3 R^{11a};
 C₆-C₁₀ aryl substituted with 0-3 R^{11b};
 C₃-C₁₀ carbocycle substituted with 0-3 R^{11b}; or
 5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen,
 oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with
 0-3 R^{11b};

R^{11a}, at each occurrence, is independently selected from H, C₁-C₆ alkyl, OR¹⁴, Cl, F, Br, I, =O,
 CN, NO₂, NR¹⁵R¹⁶, CF₃, or phenyl substituted with 0-3 R^{11b};

R^{11b}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO₂,
 NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(=O)CH₃, S(=O)₂CH₃, C₁-C₆ alkyl, C₁-C₄ alkoxy,
 C₁-C₄ haloalkyl, and C₁-C₄ haloalkoxy;

Z is C₁-C₆ alkyl substituted with 1-3 R¹²;
 C₂-C₄ alkenyl substituted with 1-3 R¹²;
 C₂-C₄ alkynyl substituted with 1-3 R¹²;
 C₆-C₁₀ aryl substituted with 0-4 R^{12b};
 C₃-C₁₀ carbocycle substituted with 0-4 R^{12b}; or
 5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen,
 oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with
 0-3 R^{12b};

R¹², at each occurrence, is independently selected from
 C₆-C₁₀ aryl substituted with 0-4 R^{12b};
 C₃-C₁₀ carbocycle substituted with 0-4 R^{12b}; or
 5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen,
 oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with
 0-3 R^{12b};

R^{12b}, at each occurrence, is independently selected from

U.S. Appl. No. 09/505,788
Response to Office Action Mailed 12/12/02
Page 38 of 93

H, OH, Cl, F, Br, I, CN, NO₂, NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(=O)CH₃, S(=O)₂CH₃,
C₁-C₆ alkyl, C₁-C₄ alkoxy, C₁-C₄ haloalkyl, and C₁-C₄ haloalkoxy;

R¹³, at each occurrence, is independently selected from
H, OH, C₁-C₆ alkyl, C₁-C₄ alkoxy, Cl, F, Br, I, CN, NO₂, NR¹⁵R¹⁶, and CF₃;

R¹⁴ is H, phenyl, benzyl, C₁-C₆ alkyl, or C₂-C₆ alkoxyalkyl;

R^{14a} is H, phenyl, benzyl, methyl, ethyl, propyl, or butyl;

R¹⁵, at each occurrence, is independently selected from H, C₁-C₆ alkyl, benzyl, phenethyl, (C₁-
C₆ alkyl)-C(=O)-, and (C₁-C₆ alkyl)-S(=O)₂-;

R¹⁶, at each occurrence, is independently selected from
H, OH, C₁-C₆ alkyl, benzyl, phenethyl,
(C₁-C₆ alkyl)-C(=O)-, and (C₁-C₆ alkyl)-S(=O)₂-;

R¹⁷ is H, C₁-C₆ alkyl, C₂-C₆ alkoxyalkyl,
aryl substituted by 0-4 R^{17a}, or
-CH₂-aryl substituted by 0-4 R^{17a};

R^{17a} is H, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, butoxy, -OH, F, Cl, Br, I,
CF₃, OCF₃, SCH₃, S(O)CH₃, SO₂CH₃, -NH₂, N(CH₃)₂, or C₁-C₄ haloalkyl;

R¹⁸, at each occurrence, is independently selected from
H, C₁-C₆ alkyl, phenyl, benzyl, phenethyl,
(C₁-C₆ alkyl)-C(=O)-, and (C₁-C₆ alkyl)-S(=O)₂-; and

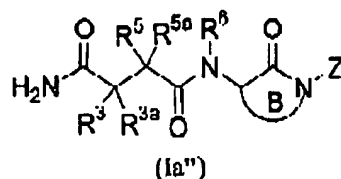
R¹⁹, at each occurrence, is independently selected from
H, OH, C₁-C₆ alkyl, phenyl, benzyl, phenethyl,
(C₁-C₆ alkyl)-C(=O)-, and (C₁-C₆ alkyl)-S(=O)₂-;

provided, when R¹³ is H,

U.S. Appl. No. 09/505,788
 Response to Office Action Mailed 12/12/02
Page 19 of 93

then Z is C₄-C₆ alkyl substituted with 1-3 R¹²;
 C₂-C₄ alkenyl substituted with 1-3 R¹²; or
 C₂-C₄ alkynyl substituted with 1-3 R¹².

14. (PREVIOUSLY AMENDED) A compound according to Claim 13 of Formula (Ia'')



or a pharmaceutically acceptable salt thereof,
 wherein:

R³ is -(CHR⁷)_n-R⁴,

n is 0 or 1;

R^{3a} is H, OH, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, butoxy, allyl, or
 3-buten-1-yl;

R⁴ is H, OH, OR^{14a},

C₁-C₄ alkyl substituted with 0-2 R^{4a},

C₂-C₄ alkenyl substituted with 0-2 R^{4a},

C₂-C₄ alkynyl substituted with 0-1 R^{4a},

C₃-C₆ carbocycle substituted with 0-3 R^{4b},

C₆-C₁₀ aryl substituted with 0-3 R^{4b}, or

5 to 6 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen,

oxygen, and sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-
 3 R^{4b};

R^{4a}, at each occurrence, is independently selected from H, F, Cl, Br, I, CF₃,

C₃-C₆ carbocycle substituted with 0-3 R^{4b},

U.S. Appl. No. 09/505,788
Response to Office Action Mailed 12/12/02
Page 40 of 93

phenyl substituted with 0-3 R^{4b}, or
5 to 6 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen,
oxygen, and sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-
3 R^{4b};

R^{4b}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO₂,
NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(=O)CH₃, S(=O)₂CH₃, C₁-C₄ alkyl, C₁-C₃ alkoxy,
C₁-C₂ haloalkyl, and C₁-C₂ haloalkoxy;

R⁵ is H, OR¹⁴;
C₁-C₄ alkyl substituted with 0-3 R^{5b};
C₂-C₄ alkenyl substituted with 0-3 R^{5b};
C₂-C₄ alkynyl substituted with 0-3 R^{5b};

R^{5a} is H, methyl, ethyl, propyl, or butyl;

R^{5b}, at each occurrence, is independently selected from:
H, methyl, ethyl, propyl, butyl, CF₃, OR¹⁴, Cl, F, Br, I, =O;
C₃-C₆ carbocycle substituted with 0-3 R^{5c};
phenyl substituted with 0-3 R^{5c}; or
5 to 6 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen,
oxygen, and sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-
3 R^{5c};

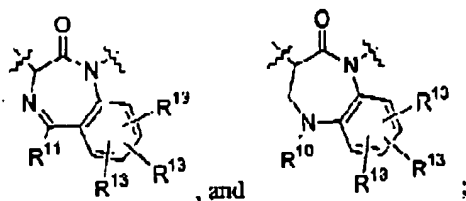
R^{5c}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO₂,
NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(=O)CH₃, S(=O)₂CH₃, C₁-C₄ alkyl, C₁-C₃ alkoxy,
C₁-C₂ haloalkyl, and C₁-C₂ haloalkoxy;

R⁶ is H;

R⁷, at each occurrence, is independently selected from H, F, CF₃, methyl, and ethyl;

Ring B is selected from

U.S. Appl. No. 09/505,788
 Response to Office Action Mailed 12/12/02
Page 41 of 93



R^{10} is H, $C(=O)R^{17}$, $C(=O)OR^{17}$;

C_1 - C_4 alkyl optionally substituted with 0-1 R^{10a} ;

phenyl substituted with 0-4 R^{10b} ;

C_3 - C_6 carbocycle substituted with 0-3 R^{10b} ; or

5 to 6 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen,

oxygen, and sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-3 R^{10b} ;

R^{10a} is selected from H, C_1 - C_4 alkyl, OR^{14} , Cl, F, Br, I, $=O$, CN, NO_2 , $NR^{15}R^{16}$, CF_3 , or phenyl substituted with 0-4 R^{10b} ;

R^{10b} , at each occurrence, is independently selected from H, OH, C_1 - C_4 alkyl, C_1 - C_3 alkoxy, Cl, F, Br, I, CN, NO_2 , $NR^{15}R^{16}$, or CF_3 ;

R^{11} is selected from

H, C_1 - C_4 alkoxy, Cl, F, $NR^{18}R^{19}$, $C(=O)R^{17}$, $C(=O)OR^{17}$, CF_3 ;

C_1 - C_6 alkyl optionally substituted with 0-3 R^{11a} ;

C_6 - C_{10} aryl substituted with 0-3 R^{11b} ;

C_3 - C_6 carbocycle substituted with 0-3 R^{11b} ; or

5 to 6 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen,

oxygen, and sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-3 R^{11b} ;

R^{11a} , at each occurrence, is independently selected from H, C_1 - C_4 alkyl, OR^{14} , F, $-O$, $NR^{15}R^{16}$, CF_3 , or phenyl substituted with 0-3 R^{11b} ;

U.S. Appl. No. 09/505,788
Response to Office Action Mailed 12/12/02
Page 42 of 93

R^{11b}, at each occurrence, is independently selected from H, OH, Cl, F, NR¹⁵R¹⁶, CF₃, C₁-C₄ alkyl, C₁-C₃ alkoxy, C₁-C₂ haloalkyl, and C₁-C₂ haloalkoxy;

Z is C₁-C₄ alkyl substituted with 1-3 R¹²;
C₂-C₄ alkenyl substituted with 1-3 R¹²;
C₂-C₄ alkynyl substituted with 1-3 R¹²;
C₆-C₁₀ aryl substituted with 0-4 R^{12b};
C₃-C₆ carbocycle substituted with 0-4 R^{12b}; or
5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-3 R^{12b};

R¹², at each occurrence, is independently selected from
C₆-C₁₀ aryl substituted with 0-4 R^{12b};
C₃-C₆ carbocycle substituted with 0-4 R^{12b}; or
5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{12b};

R^{12b}, at each occurrence, is independently selected from
H, OH, Cl, F, NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(-O)CH₃, S(=O)₂CH₃, C₁-C₄ alkyl,
C₁-C₃ alkoxy, C₁-C₂ haloalkyl, and C₁-C₂ haloalkoxy;

R¹³, at each occurrence, is independently selected from
H, OH, C₁-C₆ alkyl, C₁-C₄ alkoxy, Cl, F, Br, I, CN, NO₂, NR¹⁵R¹⁶, and CF₃;

R¹⁴ is H, phenyl, benzyl, C₁-C₄ alkyl, or C₂-C₄ alkoxyalkyl;

R¹⁵, at each occurrence, is independently selected from H, C₁-C₄ alkyl, benzyl, phenethyl, (C₁-C₄ alkyl)-C(=O)-, and (C₁-C₄ alkyl)-S(=O)₂-;

R¹⁶, at each occurrence, is independently selected from
H, OH, C₁-C₄ alkyl, benzyl, phenethyl,

U.S. Appl. No. 09/505,788
 Response to Office Action Mailed 12/12/02
Page 43 of 93

(C₁-C₄ alkyl)-C(=O)-, and (C₁-C₄ alkyl)-S(=O)₂-;

R¹⁷ is H, methyl, ethyl, propyl, butyl, methoxymethyl, ethoxymethyl, methoxyethyl, ethoxyethyl, phenyl substituted by 0-3 R^{17a}, or -CH₂-phenyl substituted by 0-3 R^{17a};

R^{17a} is H, methyl, methoxy, -OH, F, Cl, CF₃, or OCF₃;

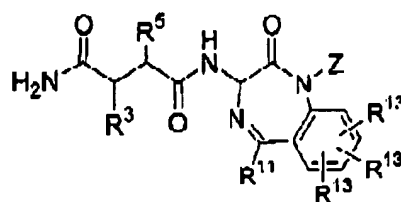
R¹⁸, at each occurrence, is independently selected from H, methyl, ethyl, propyl, butyl, phenyl, benzyl, and phenethyl; and

R¹⁹, at each occurrence, is independently selected from H, methyl, and ethyl;

provided, when R¹³ is H,
 then Z is butyl substituted with 1-3 R¹²;
 C₂-C₄ alkenyl substituted with 1-3 R¹²; or
 C₂-C₄ alkynyl substituted with 1-3 R¹².

15. (Canceled)

16. (Previously Amended) A compound according to Claim 14 of Formula (Ic):



(Ic)

or a pharmaceutically acceptable salt thereof

U.S. Appl. No. 09/505,788
 Response to Office Action Mailed 12/12/02
Page 44 of 93

wherein

R^3 is R^4 ,

R^4 is C₁-C₄ alkyl substituted with 0-1 R^{4a} ,
 C₂-C₄ alkenyl substituted with 0-1 R^{4a} , or
 C₂-C₄ alkynyl substituted with 0-1 R^{4a} ;

R^{4a} is selected from
 H, F, CF₃,
 C₃-C₆ carbocycle substituted with 0-3 R^{4b} ,
 phenyl substituted with 0-3 R^{4b} , or
 5 to 6 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen,
 oxygen, and sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-
 3 R^{4b} ; wherein said 5 to 6 membered heterocycle is selected from pyridinyl,
 pyrimidinyl, triazinyl, furanyl, thienyl, thiazolyl, pyrrolyl, piperazinyl, piperidinyl,
 pyrazolyl, imidazolyl, oxazolyl, isoxazolyl, and tetrazolyl;

R^{4b} , at each occurrence, is independently selected from H, OH, Cl, F, NR¹⁵R¹⁶, CF₃, acetyl,
 SCH₃, S(-O)CH₃, S(=O)₂CH₃, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy,
 C₁-C₂ haloalkyl, and C₁-C₂ haloalkoxy;

R^5 is C₁-C₄ alkyl substituted with 0-1 R^{5b} ,
 C₂-C₄ alkenyl substituted with 0-1 R^{5b} ,
 C₂-C₄ alkynyl substituted with 0-1 R^{5b} ;

R^{5b} is selected from:
 H, methyl, ethyl, propyl, butyl, CF₃, OR¹⁴, =O;
 C₃-C₆ carbocycle substituted with 0-2 R^{5c} ;
 phenyl substituted with 0-3 R^{5c} ; or
 5 to 6 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen,
 oxygen, and sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-
 3 R^{5c} ; wherein said 5 to 6 membered heterocycle is selected from pyridinyl,

U.S. Appl. No. 09/505,788
Response to Office Action Mailed 12/12/02
Page 45 of 93

pyrimidinyl, triazinyl, furanyl, thienyl, thiazolyl, pyrrolyl, piperazinyl, piperidinyl, pyrazolyl, imidazolyl, oxazolyl, isoxazolyl, and tetrazolyl;

R^{5c}, at each occurrence, is independently selected from H, OH, Cl, F, NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(=O)CH₃, S(=O)₂CH₃, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, C₁-C₂ haloalkyl, and C₁-C₂ haloalkoxy;

R¹¹ is selected from
H, NR¹⁸R¹⁹, CF₃;
C₁-C₄ alkyl optionally substituted with 0-1 R^{11a};
phenyl substituted with 0-3 R^{11b};
C₃-C₆ carbocycle substituted with 0-3 R^{11b}; or
5 to 6 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-3 R^{11b}; wherein said 5 to 6 membered heterocycle is selected from pyridinyl, pyrimidinyl, triazinyl, furanyl, thienyl, thiazolyl, pyrrolyl, piperazinyl, piperidinyl, pyrazolyl, imidazolyl, oxazolyl, isoxazolyl, and tetrazolyl;

R^{11a} is selected from H, C₁-C₄ alkyl, OR¹⁴, F, =O, NR¹⁵R¹⁶, CF₃, or phenyl substituted with 0-3 R^{11b};

R^{11b}, at each occurrence, is independently selected from H, OH, Cl, F, NR¹⁵R¹⁶, CF₃, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, C₁-C₂ haloalkyl, and C₁-C₂ haloalkoxy;

Z is C₁-C₃ alkyl substituted with 1-3 R¹²;
C₂-C₃ alkenyl substituted with 1-3 R¹²;
C₂-C₃ alkynyl substituted with 1-3 R¹²;
C₆-C₁₀ aryl substituted with 0-4 R^{12b};
C₃-C₆ carbocycle substituted with 0-3 R^{12b}; or
5 to 6 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-3 R^{12b}; wherein said 5 to 6 membered heterocycle is selected from pyridinyl,

U.S. Appl. No. 09/505,788
Response to Office Action Mailed 12/12/02
Page 46 of 93

pyrimidinyl, triazinyl, furanyl, thienyl, thiazolyl, pyrrolyl, piperazinyl, piperidinyl, pyrazolyl, imidazolyl, oxazolyl, isoxazolyl, and tetrazolyl;

R¹², at each occurrence, is independently selected from
C₆-C₁₀ aryl substituted with 0-4 R^{12b};
C₃-C₆ carbocycle substituted with 0-3 R^{12b}; or
5 to 6 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-3 R^{12b}; wherein said 5 to 6 membered heterocycle is selected from pyridinyl, pyrimidinyl, triazinyl, furanyl, thienyl, thiazolyl, pyrrolyl, piperazinyl, piperidinyl, pyrazolyl, imidazolyl, oxazolyl, isoxazolyl, and tetrazolyl;

R^{12b}, at each occurrence, is independently selected from
H, OH, Cl, F, NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(=O)CH₃, S(=O)₂CH₃, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, C₁-C₂ haloalkyl, and C₁-C₂ haloalkoxy;

R¹³, at each occurrence, is independently selected from
H, OH, methyl, ethyl, propyl, butyl, methoxy, ethoxy, Cl, F, Br, CN, NR¹⁵R¹⁶, and CF₃;

R¹⁴ is H, phenyl, benzyl, methyl, ethyl, propyl, or butyl;

R¹⁵, at each occurrence, is independently selected from H, methyl, ethyl, propyl, and butyl;

R¹⁶, at each occurrence, is independently selected from
H, OH, methyl, ethyl, propyl, butyl, benzyl, phenethyl, methyl-C(=O)-, ethyl-C(=O)-, methyl-S(=O)₂-, and ethyl-S(=O)₂-;

R¹⁸, at each occurrence, is independently selected from
H, methyl, ethyl, propyl, butyl, phenyl, benzyl, and phenethyl; and

R¹⁹, at each occurrence, is independently selected from
H, methyl, and ethyl;

U.S. Appl. No. 09/505,788
Response to Office Action Mailed 12/12/02
Page 47 of 93

provided, when R¹³ is H,
then Z is C₂-C₃ alkenyl substituted with 1-3 R¹²; or
C₂-C₃ alkynyl substituted with 1-3 R¹².

17. – 19. (Canceled)

20. (Currently Amended) A compound according to Claim 16, wherein:

R³ is -CH₃, -CH₂CH₃, -CH₂CH₂CH₃, -CH₂CH₂CH₂CH₃,
-CH(CH₃)₂, -CH(CH₃)CH₂CH₃, -CH₂CH(CH₃)₂,
-CH₂CF₃, -CH₂CH₂CF₃, -CH₂CH₂CH₂CF₃,
-CH=CH₂, -CH₂CH=CH₂, -CH₂C(CH₃)=CH₂,
-CH₂CH₂CH=CH₂,
cis-CH₂CH=CH(CH₃),
trans-CH₂CH=CH(CH₃),
-C≡CH, -CH₂C≡CH, -CH₂C≡C(CH₃),
cyclopropyl-CH₂-, cyclobutyl-CH₂-, cyclopentyl-CH₂-, cyclohexyl-CH₂-, cyclopropyl-
CH₂CH₂-,
cyclobutyl-CH₂CH₂-, cyclopentyl-CH₂CH₂-,
cyclohexyl-CH₂CH₂-, phenyl-CH₂-,
(2-F-phenyl)CH₂-, (3-F-phenyl)CH₂-, (4-F-phenyl)CH₂-,
(2-Cl-phenyl)CH₂-, (3-Cl-phenyl)CH₂-, (4-Cl-phenyl)CH₂-,
(2,3-diF-phenyl)CH₂-, (2,4-diF-phenyl)CH₂-,
(2,5-diF-phenyl)CH₂-, (2,6-diF-phenyl)CH₂-,
(3,4-diF-phenyl)CH₂-, (3,5-diF-phenyl)CH₂-,
(2,3-diCl-phenyl)CH₂-, (2,4-diCl-phenyl)CH₂-,
(2,5-diCl-phenyl)CH₂-, (2,6-diCl-phenyl)CH₂-,
(3,4-diCl-phenyl)CH₂-, (3,5-diCl-phenyl)CH₂-,
(3-F-4-Cl-phenyl)CH₂-, (3-F-5-Cl-phenyl)CH₂-,
(3-Cl-4-F-phenyl)CH₂-, phenyl-CH₂CH₂-,
(2-F-phenyl)CH₂CH₂-, (3-F-phenyl)CH₂CH₂-,
(4-F-phenyl)CH₂CH₂-, (2-Cl-phenyl)CH₂CH₂-,

U.S. Appl. No. 09/505,788
 Response to Office Action Mailed 12/12/02
Page 48 of 93

(3-Cl-phenyl)CH₂CH₂-, (4-Cl-phenyl)CH₂CH₂-,
 (2,3-diF-phenyl)CH₂CH₂-, (2,4-diF-phenyl)CH₂CH₂-,
 (2,5-diF-phenyl)CH₂CH₂-, (2,6-diF-phenyl)CH₂CH₂-,
 (3,4-diF-phenyl)CH₂CH₂-, (3,5-diF-phenyl)CH₂CH₂-,
 (2,3-diCl-phenyl)CH₂CH₂-, (2,4-diCl-phenyl)CH₂CH₂-,
 (2,5-diCl-phenyl)CH₂CH₂-, (2,6-diCl-phenyl)CH₂CH₂-,
 (3,4-diCl-phenyl)CH₂CH₂-, (3,5-diCl-phenyl)CH₂CH₂-,
 (3-F-4-Cl-phenyl)CH₂CH₂-, or (3-F-5-Cl-phenyl)CH₂CH₂-,

R⁵ is -CH₃, -CH₂CH₃, -CH₂CH₂CH₃, -CH(CH₃)₂, -CH₂CH₂CH₂CH₃,
 -CH(CH₃)CH₂CH₃, -CH₂CH(CH₃)₂, -CH₂C(CH₃)₃,
 -CH₂CH₂CH₂CH₂CH₃, -CH(CH₃)CH₂CH₂CH₃, -CH₂CH(CH₃)CH₂CH₃,
 -CH₂CH₂CH(CH₃)₂, -CH(CH₂CH₃)₂, -CH₂CF₃, -CH₂CH₂CF₃,
 -CH₂CH₂CH₂CF₃, -CH₂CH₂CH₂CH₂CF₃, -CH=CH₂, -CH₂CH=CH₂,
 -CH=CHCH₃, cis-CH₂CH=CH(CH₃), trans-CH₂CH=CH(CH₃),
 trans-CH₂CH=CH(C₆H₅), -CH₂CH=C(CH₃)₂, cis-CH₂CH=CHCH₂CH₃,
 trans-CH₂CH=CHCH₂CH₃, cis-CH₂CH₂CH=CH(CH₃),
 trans-CH₂CH₂CH=CH(CH₃), trans-CH₂CH=CHCH₂(C₆H₅),
 -C≡CH, -CH₂C≡CH, -CH₂C≡C(CH₃), -CH₂C≡C(C₆H₅),
 -CH₂CH₂C≡CH, -CH₂CH₂C≡C(CH₃), -CH₂CH₂C≡C(C₆H₅),
 cyclopropyl-CH₂-, cyclobutyl-CH₂-, cyclopentyl-CH₂-,
 cyclohexyl-CH₂-, (2-CH₃-cyclopropyl)CH₂-,
 (3-CH₃-cyclobutyl)CH₂-,
 cyclopropyl-CH₂CH₂-, cyclobutyl-CH₂CH₂-,
 cyclopentyl-CH₂CH₂-, cyclohexyl-CH₂CH₂-,
 (2-CH₃-cyclopropyl)CH₂CH₂-, (3-CH₃-cyclobutyl)CH₂CH₂-,
 phenyl-CH₂-, (2-F-phenyl)CH₂-, (3-F-phenyl)CH₂-,
 (4-F-phenyl)CH₂-, furanyl-CH₂-, thienyl-CH₂-,
 pyridyl-CH₂-, 1-imidazolyl-CH₂-, oxazolyl-CH₂-,
 isoxazolyl-CH₂-,
 phenyl-CH₂CH₂-, (2-F-phenyl)CH₂CH₂-, (3-F-phenyl)CH₂CH₂-,
 (4-F-phenyl)CH₂CH₂-, furanyl-CH₂CH₂-, thienyl-CH₂CH₂-,
 pyridyl-CH₂CH₂-, 1-imidazolyl-CH₂CH₂-, oxazolyl-CH₂CH₂-,
 isoxazolyl-CH₂CH₂-;

U.S. Appl. No. 09/505,788
Response to Office Action Mailed 12/12/02
Page 49 of 93

Z is phenyl, 2-F-phenyl, 3-F-phenyl, 4-F-phenyl,
2-Cl-phenyl, 3-Cl-phenyl, 4-Cl-phenyl, 2,3-diF-phenyl,
2,4-diF-phenyl, 2,5-diF-phenyl, 2,6-diF-phenyl,
3,4-diF-phenyl, 3,5-diF-phenyl, 2,3-diCl-phenyl,
2,4-diCl-phenyl, 2,5-diCl-phenyl, 2,6-diCl-phenyl,
3,4-diCl-phenyl, 3,5-diCl-phenyl, 3-F-4-Cl-phenyl,
3-F-5-Cl-phenyl, 3-Cl-4-F-phenyl, 2-MeO-phenyl,
3-MeO-phenyl, 4-MeO-phenyl, 2-Me-phenyl, 3-Me-phenyl,
4-Me-phenyl, 2-MeS-phenyl, 3-MeS-phenyl, 4-MeS-phenyl,
2-CF₃O-phenyl, 3-CF₃O-phenyl, 4-CF₃O-phenyl,
furanlyl, thienyl, pyridyl, 2-Me-pyridyl, 3-Me-pyridyl,
4-Me-pyridyl, 1-imidazolyl, oxazolyl, isoxazolyl,
cyclopropyl, cyclobutyl, cyclopentyl, cyclohexyl,
N-piperidinyl,
phenyl-CH₂-, (2-F-phenyl)CH₂-, (3-F-phenyl)CH₂-,
(4-F-phenyl)CH₂-, (2-Cl-phenyl)CH₂-, (3-Cl-phenyl)CH₂-, (4-Cl-phenyl)CH₂-, (2,3-diF-phenyl)CH₂-,
(2,4-diF-phenyl)CH₂-, (2,5-diF-phenyl)CH₂-,
(2,6-diF-phenyl)CH₂-, (3,4-diF-phenyl)CH₂-,
(3,5-diF-phenyl)CH₂-, (2,3-diCl-phenyl)CH₂-,
(2,4-diCl-phenyl)CH₂-, (2,5-diCl-phenyl)CH₂-,
(2,6-diCl-phenyl)CH₂-, (3,4-diCl-phenyl)CH₂-,
(3,5-diCl-phenyl)CH₂-, (3-F-4-Cl-phenyl)CH₂-,
(3-F-5-Cl-phenyl)CH₂-, (3-Cl-4-F-phenyl)CH₂-,
(2-MeO-phenyl)CH₂-, (3-MeO-phenyl)CH₂-,
(4-MeO-phenyl)CH₂-, (2-Me-phenyl)CH₂-,
(3-Me-phenyl)CH₂-, (4-Me-phenyl)CH₂-,
(2-MeS-phenyl)CH₂-, (3-MeS-phenyl)CH₂-,
(4-MeS-phenyl)CH₂-, (2-CF₃O-phenyl)CH₂-,
(3-CF₃O-phenyl)CH₂-, (4-CF₃O-phenyl)CH₂-,
(furanlyl)CH₂-, (thienyl)CH₂-, (pyridyl)CH₂-,
(2-Me-pyridyl)CH₂-, (3-Me-pyridyl)CH₂-,
(4-Me-pyridyl)CH₂-, (1-imidazolyl)CH₂-,

U.S. Appl. No. 09/505,788

Response to Office Action Mailed 12/12/02

Page 50 of 93

(oxazolyl)CH₂-, (isoxazolyl)CH₂-,
 (cyclopropyl)CH₂-, (cyclobutyl)CH₂-, (cyclopentyl)CH₂-,
 (cyclohexyl)CH₂-, (N-piperidiny)CH₂-,

phenyl-CH₂CH₂-, (phenyl)₂CHCH₂-, (2-F phenyl)CH₂CH₂-,
 (3-F-phenyl)CH₂CH₂-, (4-F-phenyl)CH₂CH₂-,
 (2-Cl-phenyl)CH₂CH₂-, (3-Cl-phenyl)CH₂CH₂-,
 (4-Cl-phenyl)CH₂CH₂-, (2,3-diF-phenyl)CH₂CH₂-,
 (2,4-diF-phenyl)CH₂CH₂-, (2,5-diF-phenyl)CH₂CH₂-,
 (2,6-diF-phenyl)CH₂CH₂-, (3,4-diF-phenyl)CH₂CH₂-,
 (3,5-diF-phenyl)CH₂CH₂-, (2,3-diCl phenyl)CH₂CH₂-,
 (2,4-diCl-phenyl)CH₂CH₂-, (2,5-diCl-phenyl)CH₂CH₂-,
 (2,6-diCl-phenyl)CH₂CH₂-, (3,4-diCl-phenyl)CH₂CH₂-,
 (3,5-diCl-phenyl)CH₂CH₂-, (3-F-4-Cl-phenyl)CH₂CH₂-,
 (3-F-5-Cl-phenyl)CH₂CH₂-, (3-Cl-4-F-phenyl)CH₂CH₂-,
 (2-MeO-phenyl)CH₂CH₂-, (3-MeO-phenyl)CH₂CH₂-,
 (4-MeO-phenyl)CH₂CH₂-, (2-Me-phenyl)CH₂CH₂-,
 (3-Me-phenyl)CH₂CH₂-, (4-Me-phenyl)CH₂CH₂-,
 (2-MeS-phenyl)CH₂CH₂-, (3-MeS-phenyl)CH₂CH₂-,
 (4-MeS-phenyl)CH₂CH₂-, (2-CF₃O-phenyl)CH₂CH₂-,
 (3-CF₃O-phenyl)CH₂CH₂-, (4-CF₃O-phenyl)CH₂CH₂-, (furanyl)CH₂CH₂-,
 (thienyl)CH₂CH₂-, (pyridyl)CH₂CH₂-,
 (2-Me pyridyl)CH₂CH₂-, (3-Me-pyridyl)CH₂CH₂-,
 (4-Me-pyridyl)CH₂CH₂-, (imidazolyl)CH₂CH₂-, (oxazolyl)CH₂CH₂-,
 (isoxazolyl)CH₂CH₂-, (cyclopropyl)CH₂CH₂-, (cyclobutyl)CH₂CH₂-,
 (cyclopentyl)CH₂CH₂-, (cyclohexyl)CH₂CH₂-, or
 (N-piperidiny)CH₂CH₂-;

R¹⁰ is H, methyl, ethyl, phenyl, benzyl, phenethyl,

4-F phenyl, (4-F-phenyl)CH₂-, (4-F-phenyl)CH₂CH₂-,

4-Cl-phenyl, (4-Cl-phenyl)CH₂-, (4-Cl-phenyl)CH₂CH₂-,

4-CH₃-phenyl, (4-CH₃-phenyl)CH₂-, (4-CH₃-phenyl)CH₂CH₂-,

4-CF₃-phenyl, (4-CF₃-phenyl)CH₂-, or

(4-CF₃-phenyl)CH₂CH₂-;

U.S. Appl. No. 09/505,788
Response to Office Action Mailed 12/12/02
Page 51 of 93

R¹¹, at each occurrence, is independently selected from

H, $[[=O]]$, methyl, ethyl, phenyl, benzyl, phenethyl,
4-F-phenyl, (4-F-phenyl)CH₂-, (4-F-phenyl)CH₂CH₂-,
3-F-phenyl, (3-F-phenyl)CH₂-, (3-F-phenyl)CH₂CH₂-,
2-F-phenyl, (2-F-phenyl)CH₂-, (2-F-phenyl)CH₂CH₂-,
4-Cl-phenyl, (4-Cl-phenyl)CH₂-, (4-Cl-phenyl)CH₂CH₂-,
3-Cl-phenyl, (3-Cl-phenyl)CH₂-, (3-Cl-phenyl)CH₂CH₂-,
4-CH₃-phenyl, (4-CH₃-phenyl)CH₂-, (4-CH₃-phenyl)CH₂CH₂-,
3-CH₃-phenyl, (3-CH₃-phenyl)CH₂-, (3-CH₃-phenyl)CH₂CH₂-,
4-CF₃-phenyl, (4-CF₃-phenyl)CH₂-, (4-CF₃-phenyl)CH₂CH₂-,
pyrid-2-yl, pyrid-3-yl, or pyrid-4-yl, and

R¹³, at each occurrence, is independently selected from

H, F, Cl, OH, -CH₃, -CH₂CH₃, -OCH₃, or -CF₃.

21. (Canceled)

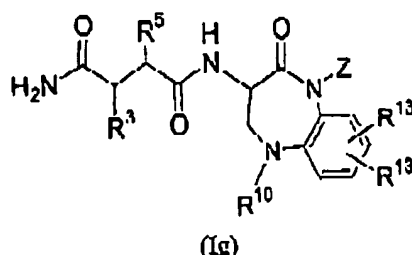
22. (Original) A pharmaceutical composition comprising a compound of Claim 1; and a pharmaceutically acceptable carrier.

23. (Previously Amended) A method for the treatment of Alzheimer's Disease comprising administering to a host in need of such treatment a therapeutically effective amount of a compound of Claim 1.

24. (Canceled)

25. (Previously added) A compound according to Claim 4 of Formula (Ig):

U.S. Appl. No. 09/505,788
 Response to Office Action Mailed 12/12/02
Page 52 of 93



(Ig)

or a pharmaceutically acceptable salt thereof wherein:

R^3 is R^4 ,

R^4 is C_1 - C_4 alkyl substituted with 0-1 R^{4a} ,
 C_2 - C_4 alkenyl substituted with 0-1 R^{4a} , or
 C_2 - C_4 alkynyl substituted with 0-1 R^{4a} ;

R^{4a} , at each occurrence, is independently selected from
 H, F, CF_3 ,
 C_3 - C_6 carbocycle substituted with 0-3 R^{4b} ,
 phenyl substituted with 0-3 R^{4b} , or
 5 to 6 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen,
 oxygen, and sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-
 3 R^{4b} ; wherein said 5 to 6 membered heterocycle is selected from pyridinyl,
 pyrimidinyl, triazinyl, furanyl, thienyl, thiazolyl, pyrrolyl, piperazinyl, piperidinyl,
 pyrazolyl, imidazolyl, oxazolyl, isoxazolyl, and tetrazolyl;

R^{4b} , at each occurrence, is independently selected from H, OH, Cl, F, $NR^{15}R^{16}$, CF_3 , acetyl,
 SCH_3 , $S(=O)CH_3$, $S(-O)_2CH_3$, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy,
 C_1 - C_2 haloalkyl, and C_1 - C_2 haloalkoxy;

R^5 is C_1 - C_4 alkyl substituted with 0-1 R^{5b} ;
 C_2 - C_4 alkenyl substituted with 0-1 R^{5b} ;
 C_2 - C_4 alkynyl substituted with 0-1 R^{5b} ;

R^{5b} is selected from:

U.S. Appl. No. 09/505,788
 Response to Office Action Mailed 12/12/02
Page 53 of 93

H, methyl, ethyl, propyl, butyl, CF₃, OR¹⁴, -O;
 C₃-C₆ carbocycle substituted with 0-2 R^{5c};
 phenyl substituted with 0-3 R^{5c}; or
 5 to 6 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen,
 oxygen, and sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-
 3 R^{5c}; wherein said 5 to 6 membered heterocycle is selected from pyridinyl,
 pyrimidinyl, triazinyl, furanyl, thienyl, thiazolyl, pyrrolyl, piperazinyl, piperidinyl,
 pyrazolyl, imidazolyl, oxazolyl, isoxazolyl, and tetrazolyl;

R^{5c}, at each occurrence, is independently selected from H, OH, Cl, F, NR¹⁵R¹⁶, CF₃, acetyl,
 SCH₃, S(=O)CH₃, S(=O)₂CH₃, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy,
 C₁-C₂ haloalkyl, and C₁-C₂ haloalkoxy;

R¹⁰ is H, C(=O)R¹⁷, C(=O)OR¹⁷;
 C₁-C₄ alkyl optionally substituted with 0-1 R^{10a};
 phenyl substituted with 0-4 R^{10b};
 C₃-C₆ carbocycle substituted with 0-3 R^{10b}; or
 5 to 6 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen,
 oxygen, and sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-
 3 R^{10b}; wherein said 5 to 6 membered heterocycle is selected from pyridinyl,
 pyrimidinyl, triazinyl, furanyl, thienyl, thiazolyl, pyrrolyl, piperazinyl, piperidinyl,
 pyrazolyl, imidazolyl, oxazolyl, isoxazolyl, and tetrazolyl;

R^{10a} is selected from H, methyl, ethyl, propyl, butyl, OR¹⁴, Cl, F, =O, NR¹⁵R¹⁶, CF₃, or
 phenyl substituted with 0-4 R^{10b};

R^{10b}, at each occurrence, is independently selected from H, OH, methyl, ethyl, propyl, butyl,
 methoxy, ethoxy, propoxy, Cl, F, NR¹⁵R¹⁶, and CF₃;

Z is H;
 C₁-C₄ alkyl substituted with 0-3 R^{12a};
 C₂-C₄ alkenyl substituted with 0-3 R^{12a}; or
 C₂-C₄ alkynyl substituted with 0-3 R^{12a};

U.S. Appl. No. 09/505,788
Response to Office Action Mailed 12/12/02
Page 54 of 93

R^{12a}, at each occurrence, is independently selected from
H, OH, Cl, F, NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(=O)CH₃, S(=O)₂CH₃, methyl, ethyl,
propyl, butyl, methoxy, ethoxy, propoxy, C₁-C₂ haloalkyl, and C₁-C₂ haloalkoxy;

R¹³, at each occurrence, is independently selected from
H, OH, methyl, ethyl, propyl, butyl, methoxy, ethoxy, Cl, F, Br, CN, NR¹⁵R¹⁶, and CF₃;

R¹⁴ is H, phenyl, benzyl, methyl, ethyl, propyl, or butyl;

R¹⁵, at each occurrence, is independently selected from H, methyl, ethyl, propyl, and butyl;

R¹⁶, at each occurrence, is independently selected from
H, OH, methyl, ethyl, propyl, butyl, benzyl, phenethyl, methyl-C(=O)-, ethyl-C(=O)-,
methyl-S(=O)₂-, and ethyl-S(=O)₂-;

R¹⁷ is H, methyl, ethyl, propyl, butyl, methoxymethyl, ethoxymethyl, methoxyethyl,
ethoxyethyl,
phenyl substituted by 0-3 R^{17a}, or
-CH₂-phenyl substituted by 0-3 R^{17a};

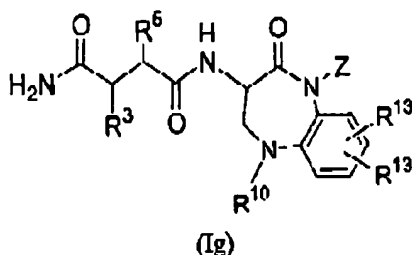
R^{17a} is H, methyl, methoxy, -OH, F, Cl, CF₃, or -OCF₃;

R¹⁸, at each occurrence, is independently selected from
H, methyl, ethyl, propyl, butyl, phenyl, benzyl, and phenethyl; and

R¹⁹, at each occurrence, is independently selected from
H, methyl, and ethyl.

26. (Previously added) A compound according to Claim 14 of Formula (1g):

U.S. Appl. No. 09/505,788
 Response to Office Action Mailed 12/12/02
Page 55 of 93



or a pharmaceutically acceptable salt thereof wherein:

R^3 is R^4 ,

R^4 is C_1 - C_4 alkyl substituted with 0-1 R^{4a} ,
 C_2 - C_4 alkenyl substituted with 0-1 R^{4a} , or
 C_2 - C_4 alkynyl substituted with 0-1 R^{4a} ;

R^{4a} is selected from

H, F, CF_3 ,

C_3 - C_6 carbocycle substituted with 0-3 R^{4b} ,

phenyl substituted with 0-3 R^{4b} , or

5 to 6 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-3 R^{4b} ; wherein said 5 to 6 membered heterocycle is selected from pyridinyl, pyrimidinyl, triazinyl, furanyl, thienyl, thiazolyl, pyrrolyl, piperazinyl, piperidinyl, pyrazolyl, imidazolyl, oxazolyl, isoxazolyl, and tetrazolyl;

R^{4b} , at each occurrence, is independently selected from H, OH, Cl, F, $NR^{15}R^{16}$, CF_3 , acetyl, SCH_3 , $S(=O)CH_3$, $S(=O)_2CH_3$, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, C_1 - C_2 haloalkyl, and C_1 - C_2 haloalkoxy;

R^5 is C_1 - C_4 alkyl substituted with 0-1 R^{5b} ;

C_2 - C_4 alkenyl substituted with 0-1 R^{5b} ;

C_2 - C_4 alkynyl substituted with 0-1 R^{5b} ;

R^{5b} is selected from:

>>

110163276v1

U.S. Appl. No. 09/505,788
 Response to Office Action Mailed 12/12/02
Page 56 of 91

H, methyl, ethyl, propyl, butyl, CF₃, OR¹⁴, =O;
 C₃-C₆ carbocycle substituted with 0-2 R^{5c};
 phenyl substituted with 0-3 R^{5c}; or
 5 to 6 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen,
 oxygen, and sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-
 3 R^{5c}, wherein said 5 to 6 membered heterocycle is selected from pyridinyl,
 pyrimidinyl, triazinyl, furanyl, thienyl, thiazolyl, pyrrolyl, piperazinyl, piperidinyl,
 pyrazolyl, imidazolyl, oxazolyl, isoxazolyl, and tetrazolyl;

R^{5c}, at each occurrence, is independently selected from H, OH, Cl, F, NR¹⁵R¹⁶, CF₃, acetyl,
 SCH₃, S(=O)CH₃, S(-O)₂CH₃, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy,
 C₁-C₂ haloalkyl, and C₁-C₂ haloalkoxy;

R¹⁰ is H, C(=O)R¹⁷, C(=O)OR¹⁷;
 C₁-C₄ alkyl optionally substituted with 0-1 R^{10a};
 phenyl substituted with 0-4 R^{10b};
 C₃-C₆ carbocycle substituted with 0-3 R^{10b}; or
 5 to 6 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen,
 oxygen, and sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-
 3 R^{10b}; wherein said 5 to 6 membered heterocycle is selected from pyridinyl,
 pyrimidinyl, triazinyl, furanyl, thienyl, thiazolyl, pyrrolyl, piperazinyl, piperidinyl,
 pyrazolyl, imidazolyl, oxazolyl, isoxazolyl, and tetrazolyl;

R^{10a} is selected from H, methyl, ethyl, propyl, butyl, OR¹⁴, Cl, F, =O, NR¹⁵R¹⁶, CF₃, or
 phenyl substituted with 0-4 R^{10b};

R^{10b}, at each occurrence, is independently selected from H, OH, methyl, ethyl, propyl, butyl,
 methoxy, ethoxy, propoxy, Cl, F, NR¹⁵R¹⁶, and CF₃;

Z is C₁-C₃ alkyl substituted with 1-3 R¹²;
 C₂-C₃ alkenyl substituted with 1-3 R¹²;
 C₂-C₃ alkynyl substituted with 1-3 R¹²;
 C₆ C₁₀ aryl substituted with 0-4 R^{12b};

U.S. Appl. No. 09/505,788
Response to Office Action Mailed 12/12/02
Page 57 of 93

C₃-C₆ carbocycle substituted with 0-3 R^{12b}; or
5 to 6 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen,
oxygen, and sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-
3 R^{12b}; wherein said 5 to 6 membered heterocycle is selected from pyridinyl,
pyrimidinyl, triazinyl, furanyl, thienyl, thiazolyl, pyrrolyl, piperazinyl, piperidinyl,
pyrazolyl, imidazolyl, oxazolyl, isoxazolyl, and tetrazolyl;

R¹², at each occurrence, is independently selected from
C₆-C₁₀ aryl substituted with 0-4 R^{12b};
C₃-C₆ carbocycle substituted with 0-3 R^{12b}; or
5 to 6 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen,
oxygen, and sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-
3 R^{12b}; wherein said 5 to 6 membered heterocycle is selected from pyridinyl,
pyrimidinyl, triazinyl, furanyl, thienyl, thiazolyl, pyrrolyl, piperazinyl, piperidinyl,
pyrazolyl, imidazolyl, oxazolyl, isoxazolyl, and tetrazolyl;

R^{12b}, at each occurrence, is independently selected from
H, OH, Cl, F, NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(=O)CH₃, S(=O)₂CH₃, methyl, ethyl,
propyl, butyl, methoxy, ethoxy, propoxy, C₁-C₂ haloalkyl, and C₁-C₂ haloalkoxy;

R¹³, at each occurrence, is independently selected from
H, OH, methyl, ethyl, propyl, butyl, methoxy, ethoxy, Cl, F, Br, CN, NR¹⁵R¹⁶, and CF₃;

R¹⁴ is H, phenyl, benzyl, methyl, ethyl, propyl, or butyl;

R¹⁵, at each occurrence, is independently selected from H, methyl, ethyl, propyl, and butyl;

R¹⁶, at each occurrence, is independently selected from
H, OH, methyl, ethyl, propyl, butyl, benzyl, phenethyl, methyl-C(=O)-, ethyl-C(=O)-,
methyl-S(=O)₂-, and ethyl-S(=O)₂-;

R¹⁷ is H, methyl, ethyl, propyl, butyl, methoxymethyl, ethoxymethyl, methoxyethyl,
ethoxyethyl,

U.S. Appl. No. 09/505,788
Response to Office Action Mailed 12/12/02
Page 58 of 93

phenyl substituted by 0-3 R^{17a}, or
CH₂-phenyl substituted by 0-3 R^{17a};

R^{17a} is H, methyl, methoxy, -OH, F, Cl, CF₃, or OCF₃;

R¹⁸, at each occurrence, is independently selected from
H, methyl, ethyl, propyl, butyl, phenyl, benzyl, and phenethyl; and

R¹⁹, at each occurrence, is independently selected from
H, methyl, and ethyl;

provided, when R¹³ is II,
then Z is C₂-C₃ alkenyl substituted with 1-3 R¹²; or
C₂-C₃ alkynyl substituted with 1-3 R¹².

27. (Previously Added) A pharmaceutical composition comprising a compound according to Claim 2 and a pharmaceutically acceptable carrier.
28. (Previously Added) A pharmaceutical composition comprising a compound according to Claim 3 and a pharmaceutically acceptable carrier.
29. (Previously Added) A pharmaceutical composition comprising a compound according to Claim 4 and a pharmaceutically acceptable carrier.
30. (Previously Added) A pharmaceutical composition comprising a compound according to Claim 6 and a pharmaceutically acceptable carrier.
31. (Canceled)
32. (Canceled)
33. (Previously Added) A pharmaceutical composition comprising a compound according to Claim 11 and a pharmaceutically acceptable carrier.

U.S. Appl. No. 09/505,788
Response to Office Action Mailed 12/12/02
Page 59 of 93

34. (Cancelled)
35. (Previously Added) A pharmaceutical composition comprising a compound according to Claim 13 and a pharmaceutically acceptable carrier.
36. (Previously Added) A pharmaceutical composition comprising a compound according to Claim 14 and a pharmaceutically acceptable carrier.
37. (Previously Added) A pharmaceutical composition comprising a compound according to Claim 16 and a pharmaceutically acceptable carrier.
38. (Cancelled)
39. (Previously Added) A pharmaceutical composition comprising a compound according to Claim 20 and a pharmaceutically acceptable carrier.
40. (Previously Added) A pharmaceutical composition comprising a compound according to Claim 25 and a pharmaceutically acceptable carrier.
41. (Previously Added) A pharmaceutical composition comprising a compound according to Claim 26 and a pharmaceutically acceptable carrier.
42. (Previously Added) A method for the treatment of Alzheimer's Disease comprising administering to a host in need of such treatment a therapeutically effective amount of a compound of Claim 2.
43. (Previously Added) A method for the treatment of Alzheimer's Disease comprising administering to a host in need of such treatment a therapeutically effective amount of a compound of Claim 3.
44. (Previously Added) A method for the treatment of Alzheimer's Disease comprising administering to a host in need of such treatment a therapeutically effective amount of a compound of Claim 4.

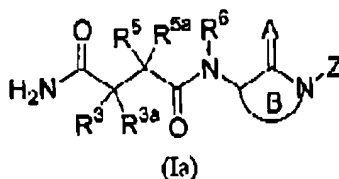
U.S. Appl. No. 09/505,788
Response to Office Action Mailed 12/12/02
Page 60 of 93

45. (Previously Added) A method for the treatment of Alzheimer's Disease comprising administering to a host in need of such treatment a therapeutically effective amount of a compound of Claim 6.
- 46.- 47. (Canceled)
48. (Previously Added) A method for the treatment of Alzheimer's Disease comprising administering to a host in need of such treatment a therapeutically effective amount of a compound of Claim 11.
49. (Canceled)
50. (Previously Added) A method for the treatment of Alzheimer's Disease comprising administering to a host in need of such treatment a therapeutically effective amount of a compound of Claim 13.
51. (Previously Added) A method for the treatment of Alzheimer's Disease comprising administering to a host in need of such treatment a therapeutically effective amount of a compound of Claim 14.
52. (Previously Added) A method for the treatment of Alzheimer's Disease comprising administering to a host in need of such treatment a therapeutically effective amount of a compound of Claim 16.
53. (Canceled)
54. (Previously Added) A method for the treatment of Alzheimer's Disease comprising administering to a host in need of such treatment a therapeutically effective amount of a compound of Claim 20.
55. (Previously Added) A method for the treatment of Alzheimer's Disease comprising administering to a host in need of such treatment a therapeutically effective amount of a compound of Claim 25.

U.S. Appl. No. 09/505,788
 Response to Office Action Mailed 12/12/02
Page 61 of 93

56. (Previously Added) A method for the treatment of Alzheimer's Disease comprising administering to a host in need of such treatment a therapeutically effective amount of a compound of Claim 26.

57. (NEW) A compound according to Claim 2 of Formula (Ia)



or a pharmaceutically acceptable salt thereof,
 wherein:

R^3 is $-(CR^7R^{7a})_n-R^4$,
 $-(CR^7R^{7a})_n-S-(CR^7R^{7a})_m-R^4$,
 $-(CR^7R^{7a})_n-O-(CR^7R^{7a})_m-R^4$, or
 $-(CR^7R^{7a})_n-N(R^{7b})-(CR^7R^{7a})_m-R^4$;

n is 0, 1, or 2;

m is 0, 1, or 2;

R^{3a} is H, OH, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, butoxy, allyl, or 3-buten-1-yl;

R^4 is H, OH, OR^{14a},
 C₁-C₆ alkyl substituted with 0-3 R^{4a},
 C₂-C₆ alkenyl substituted with 0-3 R^{4a},
 C₂-C₆ alkynyl substituted with 0-3 R^{4a},
 C₃-C₁₀ carbocycle substituted with 0-3 R^{4b},
 C₆-C₁₀ aryl substituted with 0-3 R^{4b}, or

U.S. Appl. No. 09/505,788
Response to Office Action Mailed 12/12/02
Page 62 of 93

5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{4b};

R^{4a}, at each occurrence, is independently selected from H, F, Cl, Br, I, CF₃, C₃-C₁₀ carbocycle substituted with 0-3 R^{4b}, C₆-C₁₀ aryl substituted with 0-3 R^{4b}, or 5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{4b};

R^{4b}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO₂, NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(=O)CH₃, S(=O)₂CH₃, C₁-C₆ alkyl, C₁-C₄ alkoxy, C₁-C₄ haloalkyl, and C₁-C₄ haloalkoxy;

R⁵ is H, OR¹⁴, C₁-C₆ alkyl substituted with 0-3 R^{5b}, C₁-C₆ alkoxy substituted with 0-3 R^{5b}, C₂-C₆ alkenyl substituted with 0-3 R^{5b}, C₂-C₆ alkynyl substituted with 0-3 R^{5b}, C₃-C₁₀ carbocycle substituted with 0-3 R^{5c}, C₆-C₁₀ aryl substituted with 0-3 R^{5c}; or 5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{5c};

R^{5a} is H or C₁-C₄ alkyl;

R^{5b}, at each occurrence, is independently selected from: H, C₁-C₆ alkyl, CF₃, OR¹⁴, Cl, F, Br, I, -O-, CN, NO₂, NR¹⁵R¹⁶, C₃-C₁₀ carbocycle substituted with 0-3 R^{5c}, C₆-C₁₀ aryl substituted with 0-3 R^{5c}; or

U.S. Appl. No. 09/505,788
 Response to Office Action Mailed 12/12/02
Page 63 of 93

5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{5c} ;

R^{5c} , at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2 , $NR^{15}R^{16}$, CF_3 , acetyl, SCl_3 , $S(=O)CH_3$, $S(=O)_2CH_3$, C₁-C₆ alkyl, C₁-C₄ alkoxy, C₁-C₄ haloalkyl, and C₁-C₄ haloalkoxy;

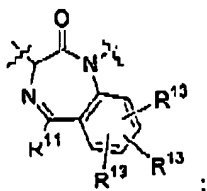
R^6 is H, methyl, or ethyl;

R^7 , at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2 , CF_3 , phenyl and C₁-C₄ alkyl;

R^{7a} , at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO_2 , CF_3 , and C₁-C₄ alkyl;

R^{7b} is independently selected from H, methyl, ethyl, propyl, and butyl;

Ring B is



R^{11} , at each occurrence, is independently selected from H, C₁-C₄ alkoxy, Cl, F, Br, I, CN, NO_2 , $NR^{18}R^{19}$, $C(=O)R^{17}$, $C(=O)OR^{17}$, $C(=O)NR^{18}R^{19}$, $S(=O)_2NR^{18}R^{19}$, CF_3 ; C₁-C₆ alkyl optionally substituted with 0-3 R^{11a} ; C₆-C₁₀ aryl substituted with 0-3 R^{11b} ; C₃-C₁₀ carbocycle substituted with 0-3 R^{11b} ; or

U.S. Appl. No. 09/505,788
Response to Office Action Mailed 12/12/02
Page 64 of 93

5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{11b};

R^{11a}, at each occurrence, is independently selected from H, C₁-C₆ alkyl, OR¹⁴, Cl, F, Br, I, =O, CN, NO₂, NR¹⁵R¹⁶, CF₃, or phenyl substituted with 0-3 R^{11b};

R^{11h}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO₂, NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(-O)CH₃, S(=O)₂CH₃, C₁-C₆ alkyl, C₁-C₄ alkoxy, C₁-C₄ haloalkyl, and C₁-C₄ haloalkoxy;

Z is H;
C₁-C₆ alkyl substituted with 0-3 R^{12a};
C₂-C₄ alkenyl substituted with 0-3 R^{12a}; or
C₂-C₄ alkynyl substituted with 0-3 R^{12a};

R^{12a}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO₂, NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(-O)CH₃, S(=O)₂CH₃, C₁-C₆ alkyl, C₁-C₄ alkoxy, C₁-C₄ haloalkyl, and C₁-C₄ haloalkoxy;

R¹³, at each occurrence, is independently selected from H, OH, C₁-C₆ alkyl, C₁-C₄ alkoxy, Cl, F, Br, I, CN, NO₂, NR¹⁵R¹⁶, and CF₃;

R¹⁴ is H, phenyl, benzyl, C₁-C₆ alkyl, or C₂-C₆ alkoxyalkyl;

R^{14a} is H, phenyl, benzyl, methyl, ethyl, propyl, or butyl;

R¹⁵, at each occurrence, is independently selected from H, C₁-C₆ alkyl, benzyl, phenethyl, (C₁-C₆ alkyl)-C(=O)-, and (C₁-C₆ alkyl)-S(=O)₂-;

R¹⁶, at each occurrence, is independently selected from H, OH, C₁-C₆ alkyl, benzyl, phenethyl, (C₁-C₆ alkyl)-C(=O)-, and (C₁-C₆ alkyl)-S(=O)₂-;

U.S. Appl. No. 09/505,788
 Response to Office Action Mailed 12/12/02
Page 65 of 93

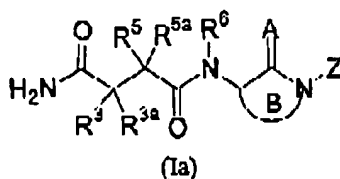
R¹⁷ is H, C₁-C₆ alkyl, C₂-C₆ alkoxyalkyl,
 aryl substituted by 0-4 R^{17a}, or
 -CH₂-aryl substituted by 0-4 R^{17a};

R^{17a} is H, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, butoxy, -OH, F, Cl, Br, I,
 CF₃, OCF₃, SCH₃, S(O)CH₃, SO₂CH₃, -NH₂, -N(CH₃)₂, or C₁-C₄ haloalkyl;

R¹⁸, at each occurrence, is independently selected from
 H, C₁-C₆ alkyl, phenyl, benzyl, phenethyl,
 (C₁-C₆ alkyl)-C(=O)-, and (C₁-C₆ alkyl)-S(-O)₂-; and

R¹⁹, at each occurrence, is independently selected from
 H, OH, C₁-C₆ alkyl, phenyl, benzyl, phenethyl,
 (C₁-C₆ alkyl)-C(=O)-, and (C₁-C₆ alkyl)-S(=O)₂-.

58. (NEW) A compound according to Claim 2 of Formula (Ia)



or a pharmaceutically acceptable salt thereof,
 wherein:

R³ is -(CR⁷R^{7a})_n-R⁴,
 -(CR⁷R^{7a})_n-S-(CR⁷R^{7a})_m-R⁴,
 -(CR⁷R^{7a})_n-O-(CR⁷R^{7a})_m-R⁴, or
 -(CR⁷R^{7a})_n-N(R^{7b})-(CR⁷R^{7a})_m-R⁴;

n is 0, 1, or 2;

U.S. Appl. No. 09/505,788
Response to Office Action Mailed 12/12/02
Page 66 of 93

m is 0, 1, or 2;

R^{3a} is H, OH, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, butoxy, allyl, or 3-buten-1-yl;

R⁴ is H, OH, OR^{14a},

C₁-C₆ alkyl substituted with 0-3 R^{4a},

C₂-C₆ alkenyl substituted with 0-3 R^{4a},

C₂-C₆ alkynyl substituted with 0-3 R^{4a},

C₃-C₁₀ carbocycle substituted with 0-3 R^{4b},

C₆-C₁₀ aryl substituted with 0-3 R^{4b}, or

5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{4b};

R^{4a}, at each occurrence, is independently selected from H, F, Cl, Br, I, CF₃,

C₃-C₁₀ carbocycle substituted with 0-3 R^{4b},

C₆-C₁₀ aryl substituted with 0-3 R^{4b}, or

5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{4b};

R^{4b}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO₂,

NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(=O)CH₃, S(=O)₂CH₃, C₁-C₆ alkyl, C₁-C₄ alkoxy,

C₁-C₄ haloalkyl, and C₁-C₄ haloalkoxy;

R⁵ is H, OR¹⁴,

C₁-C₆ alkyl substituted with 0-3 R^{5b};

C₁-C₆ alkoxy substituted with 0-3 R^{5b};

C₂-C₆ alkenyl substituted with 0-3 R^{5b};

C₂-C₆ alkynyl substituted with 0-3 R^{5b};

C₃-C₁₀ carbocycle substituted with 0-3 R^{5c};

C₆-C₁₀ aryl substituted with 0-3 R^{5c}; or

U.S. Appl. No. 09/505,788
Response to Office Action Mailed 12/12/02
Page 67 of 93

5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{5c};

R^{5a} is H or C₁-C₄ alkyl;

R^{5b}, at each occurrence, is independently selected from:
H, C₁-C₆ alkyl, CF₃, OR¹⁴, Cl, F, Br, I, =O, CN, NO₂, NR¹⁵R¹⁶;
C₃-C₁₀ carbocycle substituted with 0-3 R^{5c};
C₆-C₁₀ aryl substituted with 0-3 R^{5c}; or
5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{5c};

R^{5c}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO₂, NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(=O)CH₃, S(=O)₂CH₃, C₁-C₆ alkyl, C₁-C₄ alkoxy, C₁-C₄ haloalkyl, and C₁-C₄ haloalkoxy;

R⁶ is H, methyl, or ethyl;

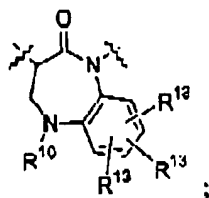
R⁷, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO₂, CF₃, phenyl and C₁-C₄ alkyl;

R^{7a}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO₂, CF₃, and C₁-C₄ alkyl;

R^{7b} is independently selected from H, methyl, ethyl, propyl, and butyl;

Ring B is

U.S. Appl. No. 09/505,788
 Response to Office Action Mailed 12/12/02
Page 68 of 93



R^{10} is H, $C(=O)R^{17}$, $C(=O)OR^{17}$, $C(=O)NR^{18}R^{19}$,

$S(=O)_2NR^{18}R^{19}$, $S(=O)_2R^{17}$;

C_1 - C_6 alkyl optionally substituted with 0-2 R^{10a} ;

C_6 - C_{10} aryl substituted with 0-4 R^{10b} ;

C_3 - C_{10} carbocycle substituted with 0-3 R^{10b} ; or

5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{10b} ;

R^{10a} , at each occurrence, is independently selected from H, C_1 - C_6 alkyl, OR^{14} , Cl, F, Br, I, $-O-$, CN, NO_2 , $NR^{15}R^{16}$, CF_3 , or phenyl substituted with 0-4 R^{10b} ;

R^{10b} , at each occurrence, is independently selected from H, OH, C_1 - C_6 alkyl, C_1 - C_4 alkoxy, Cl, F, Br, I, CN, NO_2 , $NR^{15}R^{16}$, or CF_3 ;

Z is H;

C_1 - C_6 alkyl substituted with 0-3 R^{12a} ;

C_2 - C_4 alkenyl substituted with 0-3 R^{12a} ; or

C_2 - C_4 alkynyl substituted with 0-3 R^{12a} ;

R^{12a} , at each occurrence, is independently selected from

H, OH, Cl, F, Br, I, CN, NO_2 , $NR^{15}R^{16}$, CF_3 , methyl, SCl_2 , $S(=O)CH_3$, $S(=O)_2CH_3$,

C_1 - C_6 alkyl, C_1 - C_4 alkoxy, C_1 - C_4 haloalkyl, and C_1 - C_4 haloalkoxy;

R^{13} , at each occurrence, is independently selected from

U.S. Appl. No. 09/505,788
 Response to Office Action Mailed 12/12/02
Page 69 of 93

H, OH, C₁-C₆ alkyl, C₁-C₄ alkoxy, Cl, F, Br, I, CN, NO₂, NR¹⁵R¹⁶, and CF₃;

R¹⁴ is H, phenyl, benzyl, C₁-C₆ alkyl, or C₂-C₆ alkoxyalkyl;

R^{14a} is H, phenyl, benzyl, methyl, ethyl, propyl, or butyl;

R¹⁵, at each occurrence, is independently selected from H, C₁-C₆ alkyl, benzyl, phenethyl, (C₁-C₆ alkyl)-C(=O)-, and (C₁-C₆ alkyl)-S(=O)₂;

R¹⁶, at each occurrence, is independently selected from
 H, OH, C₁-C₆ alkyl, benzyl, phenethyl,
 (C₁-C₆ alkyl)-C(=O)-, and (C₁-C₆ alkyl)-S(=O)₂;

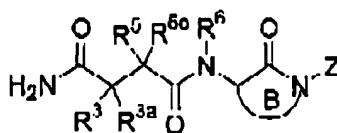
R¹⁷ is H, C₁-C₆ alkyl, C₂-C₆ alkoxyalkyl,
 aryl substituted by 0-4 R^{17a}, or
 -CH₂-aryl substituted by 0-4 R^{17a};

R^{17a} is H, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, butoxy, -OH, F, Cl, Br, I, CF₃, OCF₃, SCH₃, S(O)CH₃, SO₂CH₃, -NH₂, -N(CH₃)₂, or C₁-C₄ haloalkyl;

R¹⁸, at each occurrence, is independently selected from
 H, C₁-C₆ alkyl, phenyl, benzyl, phenethyl,
 (C₁-C₆ alkyl)-C(=O)-, and (C₁-C₆ alkyl)-S(=O)₂; and

R¹⁹, at each occurrence, is independently selected from
 H, OH, C₁-C₆ alkyl, phenyl, benzyl, phenethyl,
 (C₁-C₆ alkyl)-C(=O)-, and (C₁-C₆ alkyl)-S(=O)₂.

59. (NEW) A compound according to Claim 12 of Formula (Iaⁿ)



U.S. Appl. No. 09/505,788
 Response to Office Action Mailed 12/12/02
Page 70 of 93

(1a'')

or a pharmaceutically acceptable salt thereof,
 wherein:

R³ is -(CR⁷R^{7a})_n-R⁴,
 -(CR⁷R^{7a})_n-S-(CR⁷R^{7a})_m-R⁴,
 -(CR⁷R^{7a})_n-O-(CR⁷R^{7a})_m-R⁴, or
 -(CR⁷R^{7a})_n-N(R^{7b})-(CR⁷R^{7a})_m-R⁴;

n is 0, 1, or 2;

m is 0, 1, or 2;

R^{3a} is H, OH, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, butoxy, allyl, or 3-buten-1-yl;

R⁴ is H, OH, OR^{14a},
 C₁-C₆ alkyl substituted with 0-3 R^{4a},
 C₂-C₆ alkenyl substituted with 0-3 R^{4a},
 C₂-C₆ alkynyl substituted with 0-3 R^{4a},
 C₃-C₁₀ carbocycle substituted with 0-3 R^{4b},
 C₆-C₁₀ aryl substituted with 0-3 R^{4b}, or
 5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{4b};

R^{4a}, at each occurrence, is independently selected from H, F, Cl, Br, I, CF₃,

C₃-C₁₀ carbocycle substituted with 0-3 R^{4b},
 C₆-C₁₀ aryl substituted with 0-3 R^{4b}, or

U.S. Appl. No. 09/505,788
 Response to Office Action Mailed 12/12/02
Page 71 of 93

5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{4b};

R^{4b}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO₂, NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(-O)CH₃, S(=O)₂CH₃, C₁-C₆ alkyl, C₁-C₄ alkoxy, C₁-C₄ haloalkyl, and C₁-C₄ haloalkoxy;

R⁵ is H, OR¹⁴;

C₁-C₆ alkyl substituted with 0-3 R^{5b};

C₁-C₆ alkoxy substituted with 0-3 R^{5b};

C₂-C₆ alkenyl substituted with 0-3 R^{5b};

C₂-C₆ alkynyl substituted with 0-3 R^{5b};

C₃-C₁₀ carbocycle substituted with 0-3 R^{5c};

C₆-C₁₀ aryl substituted with 0-3 R^{5c}; or

5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{5c};

R^{5a} is H or C₁-C₄ alkyl;

R^{5b}, at each occurrence, is independently selected from:

H, C₁-C₆ alkyl, CF₃, OR¹⁴, Cl, F, Br, I, -O, CN, NO₂, NR¹⁵R¹⁶;

C₃-C₁₀ carbocycle substituted with 0-3 R^{5c};

C₆-C₁₀ aryl substituted with 0-3 R^{5c}; or

5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{5c};

R^{5c}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO₂,

NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(=O)CH₃, S(=O)₂CH₃, C₁-C₆ alkyl, C₁-C₄ alkoxy,

C₁-C₄ haloalkyl, and C₁-C₄ haloalkoxy;

U.S. Appl. No. 09/505,788
 Response to Office Action Mailed 12/12/02
Page 72 of 93

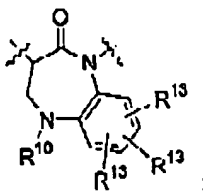
R⁶ is H, methyl, or ethyl;

R⁷, at each occurrence, is independently selected from
 H, OH, Cl, F, Br, I, CN, NO₂, CF₃, phenyl, and C₁-C₄ alkyl;

R^{7a}, at each occurrence, is independently selected from
 H, OH, Cl, F, Br, I, CN, NO₂, CF₃, and C₁-C₄ alkyl;

R^{7b} is independently selected from H, methyl, ethyl, propyl, and butyl;

Ring B is



R¹⁰ is H, C(=O)R¹⁷, C(=O)OR¹⁷, C(=O)NR¹⁸R¹⁹,
 S(=O)₂NR¹⁸R¹⁹, S(=O)₂R¹⁷;
 C₁-C₆ alkyl optionally substituted with 0-2 R^{10a};
 C₆-C₁₀ aryl substituted with 0-4 R^{10b};
 C₃-C₁₀ carbocycle substituted with 0-3 R^{10b}; or
 5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen,
 oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with
 0-3 R^{10b};

R^{10a}, at each occurrence, is independently selected from H, C₁-C₆ alkyl, OR¹⁴, Cl, F, Br, I, =O,
 CN, NO₂, NR¹⁵R¹⁶, CF₃, or phenyl substituted with 0-4 R^{10b};

R^{10b}, at each occurrence, is independently selected from H, OH, C₁-C₆ alkyl, C₁-C₄ alkoxy,
 Cl, F, Br, I, CN, NO₂, NR¹⁵R¹⁶, or CF₃;

U.S. Appl. No. 09/505,788
Response to Office Action Mailed 12/12/02
Page 73 of 93

R¹¹, at each occurrence, is independently selected from
H, C₁-C₄ alkoxy, Cl, F, Br, I, CN, NO₂, NR¹⁸R¹⁹, C(=O)R¹⁷, C(=O)OR¹⁷,
C(=O)NR¹⁸R¹⁹, S(=O)₂NR¹⁸R¹⁹, CF₃;
C₁-C₆ alkyl optionally substituted with 0-3 R^{11a};
C₆-C₁₀ aryl substituted with 0-3 R^{11b};
C₃-C₁₀ carbocycle substituted with 0-3 R^{11b}; or
5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen,
oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with
0-3 R^{11b};

R^{11a}, at each occurrence, is independently selected from H, C₁-C₆ alkyl, OR¹⁴, Cl, F, Br, I, =O,
CN, NO₂, NR¹⁵R¹⁶, CF₃, or phenyl substituted with 0-3 R^{11b};

R^{11b}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO₂,
NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(=O)CH₃, S(=O)₂CH₃, C₁-C₆ alkyl, C₁-C₄ alkoxy,
C₁-C₄ haloalkyl, and C₁-C₄ haloalkoxy;

Z is C₁-C₆ alkyl substituted with 1-3 R¹²;
C₂-C₄ alkenyl substituted with 1-3 R¹²;
C₂-C₄ alkynyl substituted with 1-3 R¹²;
C₆-C₁₀ aryl substituted with 0-4 R^{12b};
C₃-C₁₀ carbocycle substituted with 0-4 R^{12b}; or
5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen,
oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with
0-3 R^{12b};

R¹², at each occurrence, is independently selected from
C₆-C₁₀ aryl substituted with 0-4 R^{12b};
C₃-C₁₀ carbocycle substituted with 0-4 R^{12b}; or
5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen,
oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with
0-3 R^{12b};

U.S. Appl. No. 09/505,788
Response to Office Action Mailed 12/17/02
Page 74 of 93

R^{12b}, at each occurrence, is independently selected from
H, OH, Cl, F, Br, I, CN, NO₂, NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(=O)CH₃, S(=O)₂CH₃,
C₁-C₆ alkyl, C₁-C₄ alkoxy, C₁-C₄ haloalkyl, and C₁-C₄ haloalkoxy;

R¹³, at each occurrence, is independently selected from
H, OH, C₁-C₆ alkyl, C₁-C₄ alkoxy, Cl, F, Br, I, CN, NO₂, NR¹⁵R¹⁶, and CF₃;

R¹⁴ is H, phenyl, benzyl, C₁-C₆ alkyl, or C₂-C₆ alkoxyalkyl;

R^{14a} is H, phenyl, benzyl, methyl, ethyl, propyl, or butyl;

R¹⁵, at each occurrence, is independently selected from H, C₁-C₆ alkyl, benzyl, phenethyl, (C₁-
C₆ alkyl)-C(=O)-, and (C₁-C₆ alkyl)-S(=O)₂-;

R¹⁶, at each occurrence, is independently selected from
H, OH, C₁-C₆ alkyl, benzyl, phenethyl,
(C₁-C₆ alkyl)-C(=O)-, and (C₁-C₆ alkyl)-S(=O)₂-;

R¹⁷ is H, C₁-C₆ alkyl, C₂-C₆ alkoxyalkyl,
aryl substituted by 0-4 R^{17a}, or
-CH₂ aryl substituted by 0-4 R^{17a};

R^{17a} is H, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, butoxy, -OH, F, Cl, Br, I,
CF₃, OCF₃, SCH₃, S(O)CH₃, SO₂CH₃, -NH₂, -N(CH₃)₂, or C₁-C₄ haloalkyl;

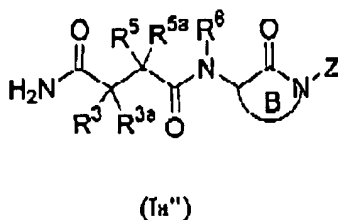
R¹⁸, at each occurrence, is independently selected from
H, C₁-C₆ alkyl, phenyl, benzyl, phenethyl,
(C₁-C₆ alkyl)-C(=O)-, and (C₁-C₆ alkyl)-S(=O)₂-; and

R¹⁹, at each occurrence, is independently selected from
H, OH, C₁-C₆ alkyl, phenyl, benzyl, phenethyl,
(C₁-C₆ alkyl)-C(=O)-, and (C₁-C₆ alkyl)-S(=O)₂-;

U.S. Appl. No. 09/505,788
 Response to Office Action Mailed 12/12/02
Page 75 of 93

provided, when R¹³ is H,
 then Z is C₄-C₆ alkyl substituted with 1-3 R¹²;
 C₂-C₄ alkenyl substituted with 1-3 R¹²; or
 C₂-C₄ alkynyl substituted with 1-3 R¹².

60. (NEW) A compound according to Claim 12 of Formula (Ia'')



or a pharmaceutically acceptable salt thereof,
 wherein:

R³ is -(CR⁷R^{7a})_n-R⁴,
 -(CR⁷R^{7a})_n-S-(CR⁷R^{7a})_m-R⁴,
 -(CR⁷R^{7a})_n-O-(CR⁷R^{7a})_m-R⁴, or
 -(CR⁷R^{7a})_n-N(R^{7b})-(CR⁷R^{7a})_m-R⁴;

n is 0, 1, or 2;

m is 0, 1, or 2;

R^{3a} is H, OH, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, butoxy, allyl, or 3-buten-1-yl;

R⁴ is H, OH, OR^{14a},
 C₁-C₆ alkyl substituted with 0-3 R^{4a},
 C₂-C₆ alkenyl substituted with 0-3 R^{4a},

U.S. Appl. No. 09/505,788
Response to Office Action Mailed 12/12/02
Page 76 of 93

C₂-C₆ alkynyl substituted with 0-3 R^{4a},
C₃-C₁₀ carbocycle substituted with 0-3 R^{4b},
C₆-C₁₀ aryl substituted with 0-3 R^{4b}, or
5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen,
oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with
0-3 R^{4b};

R^{4a}, at each occurrence, is independently selected from H, F, Cl, Br, I, CF₃,
C₃-C₁₀ carbocycle substituted with 0-3 R^{4h},
C₆-C₁₀ aryl substituted with 0-3 R^{4b}, or
5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen,
oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with
0-3 R^{4h};

R^{4b}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO₂,
NR¹⁵R¹⁶, CF₃, acetyl, SOH₃, S(=O)CH₃, S(=O)₂CH₃, C₁-C₆ alkyl, C₁-C₄ alkoxy,
C₁-C₄ haloalkyl, and C₁-C₄ haloalkoxy;

R⁵ is H, OR¹⁴,
C₁-C₆ alkyl substituted with 0-3 R^{5b},
C₁-C₆ alkoxy substituted with 0-3 R^{5b},
C₂-C₆ alkenyl substituted with 0-3 R^{5b},
C₂-C₆ alkynyl substituted with 0-3 R^{5b},
C₃-C₁₀ carbocycle substituted with 0-3 R^{5c},
C₆-C₁₀ aryl substituted with 0-3 R^{5c}; or
5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen,
oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with
0-3 R^{5c};

R^{5a} is H or C₁-C₄ alkyl;

R^{5b}, at each occurrence, is independently selected from:
H, C₁-C₆ alkyl, CF₃, OR¹⁴, Cl, F, Br, I, -O-, CN, NO₂, NR¹⁵R¹⁶;

U.S. Appl. No. 09/505,788
 Response to Office Action Mailed 12/12/02
Page 77 of 93

C₃-C₁₀ carbocycle substituted with 0-3 R^{5c};

C₆-C₁₀ aryl substituted with 0-3 R^{5c}; or

5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{5c};

R^{5c}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO₂,

NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(=O)CH₃, S(=O)₂CH₃, C₁-C₆ alkyl, C₁-C₄ alkoxy, C₁-C₄ haloalkyl, and C₁-C₄ haloalkoxy;

R⁶ is H, methyl, or ethyl;

R⁷, at each occurrence, is independently selected from

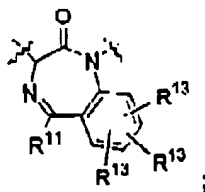
H, OH, Cl, F, Br, I, CN, NO₂, CF₃, phenyl, and C₁-C₄ alkyl;

R^{7a}, at each occurrence, is independently selected from

H, OH, Cl, F, Br, I, CN, NO₂, CF₃, and C₁-C₄ alkyl;

R^{7b} is independently selected from H, methyl, ethyl, propyl, and butyl;

Ring B is



R¹¹, at each occurrence, is independently selected from

H, C₁-C₄ alkoxy, Cl, F, Br, I, CN, NO₂, NR¹⁸R¹⁹, C(=O)R¹⁷, C(=O)OR¹⁷,

C(=O)NR¹⁸R¹⁹, S(=O)₂NR¹⁸R¹⁹, CF₃;

C₁-C₆ alkyl optionally substituted with 0-3 R^{11a};

U.S. Appl. No. 09/505,788
Response to Office Action Mailed 12/12/02
Page 78 of 93

C₆-C₁₀ aryl substituted with 0-3 R^{11b};
C₃-C₁₀ carbocycle substituted with 0-3 R^{11b}; or
5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen,
oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with
0-3 R^{11b};

R^{11a}, at each occurrence, is independently selected from H, C₁-C₆ alkyl, OR¹⁴, Cl, F, Br, I, -O,
CN, NO₂, NR¹⁵R¹⁶, CF₃, or phenyl substituted with 0-3 R^{11b};

R^{11b}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO₂,
NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(=O)CH₃, S(=O)₂CH₃, C₁-C₆ alkyl, C₁-C₄ alkoxy,
C₁-C₄ haloalkyl, and C₁-C₄ haloalkoxy;

Z is C₁-C₆ alkyl substituted with 1-3 R¹²;
C₂-C₄ alkenyl substituted with 1-3 R¹²;
C₂-C₄ alkynyl substituted with 1-3 R¹²;
C₆-C₁₀ aryl substituted with 0-4 R^{12b};
C₃-C₁₀ carbocycle substituted with 0-4 R^{12b}; or
5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen,
oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with
0-4 R^{12b};

R¹², at each occurrence, is independently selected from
C₆-C₁₀ aryl substituted with 0-4 R^{12b};
C₃-C₁₀ carbocycle substituted with 0-4 R^{12b}; or
5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen,
oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with
0-3 R^{12b};

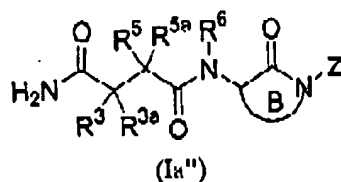
R^{12b}, at each occurrence, is independently selected from
H, OH, Cl, F, Br, I, CN, NO₂, NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(=O)CH₃, S(=O)₂CH₃,
C₁-C₆ alkyl, C₁-C₄ alkoxy, C₁-C₄ haloalkyl, and C₁-C₄ haloalkoxy;

U.S. Appl. No. 09/505,788
Response to Office Action Mailed 12/12/02
Page 79 of 93

- R¹³, at each occurrence, is independently selected from
H, OH, C₁-C₆ alkyl, C₁-C₄ alkoxy, Cl, F, Br, I, CN, NO₂, NR¹⁵R¹⁶, and CF₃;
- R¹⁴ is H, phenyl, benzyl, C₁-C₆ alkyl, or C₂-C₆ alkoxyalkyl;
- R^{14a} is H, phenyl, benzyl, methyl, ethyl, propyl, or butyl;
- R¹⁵, at each occurrence, is independently selected from H, C₁-C₆ alkyl, benzyl, phenethyl, (C₁-C₆ alkyl)-C(=O)-, and (C₁-C₆ alkyl)-S(=O)₂-;
- R¹⁶, at each occurrence, is independently selected from
H, OH, C₁-C₆ alkyl, benzyl, phenethyl,
(C₁-C₆ alkyl)-C(=O)-, and (C₁-C₆ alkyl)-S(=O)₂-;
- R¹⁷ is H, C₁-C₆ alkyl, C₂-C₆ alkoxyalkyl,
aryl substituted by 0-4 R^{17a}, or
-CH₂-aryl substituted by 0-4 R^{17a};
- R^{17a} is H, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, butoxy, -OH, F, Cl, Br, I,
CF₃, OCF₃, SCH₃, S(O)CH₃, SO₂CH₃, -NH₂, -N(CH₃)₂, or C₁-C₄ haloalkyl;
- R¹⁸, at each occurrence, is independently selected from
H, C₁-C₆ alkyl, phenyl, benzyl, phenethyl,
(C₁-C₆ alkyl)-C(=O)-, and (C₁-C₆ alkyl)-S(=O)₂-; and
- R¹⁹, at each occurrence, is independently selected from
H, OH, C₁-C₆ alkyl, phenyl, benzyl, phenethyl,
(C₁-C₆ alkyl)-C(=O)-, and (C₁-C₆ alkyl)-S(=O)₂-;
- provided, when R¹³ is H,
then Z is C₄-C₆ alkyl substituted with 1-3 R¹²;
C₂-C₄ alkenyl substituted with 1-3 R¹²; or
C₂-C₄ alkynyl substituted with 1-3 R¹².

U.S. Appl. No. 09/505,788
 Response to Office Action Mailed 12/12/02
Page 80 of 93

61. (NEW) A compound according to Claim 13 of Formula (Ia'')



or a pharmaceutically acceptable salt thereof,
 wherein:

R^3 is $(CHR^7)_n-R^4$,

n is 0 or 1;

R^{3a} is H, OH, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, butoxy, allyl, or
 3-buten-1-yl;

R^4 is H, OH, OR^{14a},

C₁-C₄ alkyl substituted with 0-2 R^{4a} ,

C₂-C₄ alkenyl substituted with 0-2 R^{4a} ,

C₂-C₄ alkynyl substituted with 0-1 R^{4a} ,

C₃-C₆ carbocycle substituted with 0-3 R^{4b} ,

C₆-C₁₀ aryl substituted with 0-3 R^{4b} , or

5 to 6 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen,
 oxygen, and sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-
 3 R^{4b} ;

R^{1a} , at each occurrence, is independently selected from H, F, Cl, Br, I, CF₃,

C₃-C₆ carbocycle substituted with 0-3 R^{4b} ,

phenyl substituted with 0-3 R^{4b} , or

U.S. Appl. No. 09/505,788
Response to Office Action Mailed 12/12/02
Page 81 of 93

5 to 6 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-3 R^{4b};

R^{4b}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO₂, NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(=O)CH₃, S(=O)₂CH₃, C₁-C₄ alkyl, C₁-C₃ alkoxy, C₁-C₂ haloalkyl, and C₁-C₂ haloalkoxy;

R⁵ is H, OR¹⁴;
C₁-C₄ alkyl substituted with 0-3 R^{5b};
C₂-C₄ alkenyl substituted with 0-3 R^{5b};
C₂-C₄ alkynyl substituted with 0-3 R^{5b};

R^{5a} is H, methyl, ethyl, propyl, or butyl;

R^{5b}, at each occurrence, is independently selected from:
H, methyl, ethyl, propyl, butyl, CF₃, OR¹⁴, Cl, F, Br, I, =O;
C₃-C₆ carbocycle substituted with 0-3 R^{5c};
phenyl substituted with 0-3 R^{5c}; or
5 to 6 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-3 R^{5c};

R^{5c}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO₂, NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(=O)CH₃, S(=O)₂CH₃, C₁-C₄ alkyl, C₁-C₃ alkoxy, C₁-C₂ haloalkyl, and C₁-C₂ haloalkoxy;

R⁶ is H;

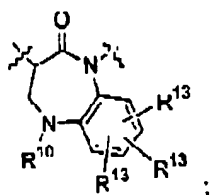
R⁷, at each occurrence, is independently selected from H, F, CF₃, methyl, and ethyl;

Ring B is

U.S. Appl. No. 09/505,788

Response to Office Action Mailed 12/12/02

Page 82 of 93



R^{10} is H, $C(=O)R^{17}$, $C(=O)OR^{17}$;

C_1 - C_4 alkyl optionally substituted with 0-1 R^{10a} ;

phenyl substituted with 0-4 R^{10b} ;

C_3 - C_6 carbocycle substituted with 0-3 R^{10b} ; or

5 to 6 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-3 R^{10b} ;

R^{10a} is selected from H, C_1 - C_4 alkyl, OR^{14} , Cl, F, Br, I, $=O$, CN, NO_2 , $NR^{15}R^{16}$, CF_3 , or phenyl substituted with 0-4 R^{10b} ;

R^{10b} , at each occurrence, is independently selected from H, OH, C_1 - C_4 alkyl, C_1 - C_3 alkoxy, Cl, F, Br, I, CN, NO_2 , $NR^{15}R^{16}$, or CF_3 ;

Z is C_1 - C_4 alkyl substituted with 1-3 R^{12} ;

C_2 - C_4 alkenyl substituted with 1-3 R^{12} ;

C_2 - C_4 alkynyl substituted with 1-3 R^{12} ;

C_6 - C_{10} aryl substituted with 0-4 R^{12b} ;

C_3 - C_6 carbocycle substituted with 0-4 R^{12b} ; or

5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-3 R^{12b} ;

R^{12} , at each occurrence, is independently selected from

C_6 - C_{10} aryl substituted with 0-4 R^{12b} ;

C_3 - C_6 carbocycle substituted with 0-4 R^{12b} ; or

U.S. Appl. No. 09/505,788
Response to Office Action Mailed 12/12/02
Page 83 of 93

5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{12b};

R^{12b}, at each occurrence, is independently selected from H, OH, Cl, F, NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(=O)CH₃, S(-O)₂CH₃, C₁-C₄ alkyl, C₁-C₃ alkoxy, C₁-C₂ haloalkyl, and C₁-C₂ haloalkoxy;

R¹³, at each occurrence, is independently selected from H, OH, C₁-C₆ alkyl, C₁-C₄ alkoxy, Cl, F, Br, I, CN, NO₂, NR¹⁵R¹⁶, and CF₃;

R¹⁴ is H, phenyl, benzyl, C₁-C₄ alkyl, or C₂-C₄ alkoxyalkyl;

R¹⁵, at each occurrence, is independently selected from H, C₁-C₄ alkyl, benzyl, phenethyl, (C₁-C₄ alkyl)-C(=O)-, and (C₁-C₄ alkyl)-S(=O)₂-;

R¹⁶, at each occurrence, is independently selected from H, OH, C₁-C₄ alkyl, benzyl, phenethyl, (C₁-C₄ alkyl)-C(=O)-, and (C₁-C₄ alkyl)-S(=O)₂-;

R¹⁷ is H, methyl, ethyl, propyl, butyl, methoxymethyl, ethoxymethyl, methoxyethyl, ethoxyethyl, phenyl substituted by 0-3 R^{17a}, or -CH₂-phenyl substituted by 0-3 R^{17a};

R^{17a} is H, methyl, methoxy, -OH, F, Cl, CF₃, or OCF₃;

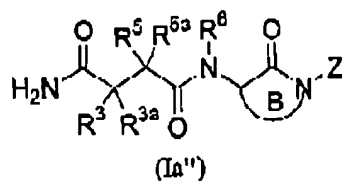
R¹⁸, at each occurrence, is independently selected from H, methyl, ethyl, propyl, butyl, phenyl, benzyl, and phenethyl; and

R¹⁹, at each occurrence, is independently selected from H, methyl, and ethyl;

U.S. Appl. No. 09/505,788
Response to Office Action Mailed 12/12/02
Page 84 of 93

provided, when R¹³ is H,
then Z is butyl substituted with 1-3 R¹²;
C₂-C₄ alkanyl substituted with 1-3 R¹²; or
C₂-C₄ alkynyl substituted with 1-3 R¹².

62. (NEW) A compound according to Claim 13 of Formula (Ia")



or a pharmaceutically acceptable salt thereof,
wherein:

$$R^3 \text{ is } -(CHR^7)_m-R^4,$$

n is 0 or 1;

R^{3a} is H, OH, methyl, ethyl, propyl, butyl, methoxy, ethoxy, propoxy, butoxy, allyl, or 3-buten-1-yl;

R^4 is H, OH, OR^{14a},

C1-C4 alkyl substituted with 0-2 R^{4a},
C2-C4 alkenyl substituted with 0-2 R^{4a},
C2-C4 alkynyl substituted with 0-1 R^{4a},
C3-C₆ carbocycle substituted with 0-3 R^{4b},
C6-C₁₀ aryl substituted with 0-3 R^{4b}, or

U.S. Appl. No. 09/505,788
Response to Office Action Mailed 12/12/02
Page 85 of 93

5 to 6 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-3 R^{4b};

R^{4a}, at each occurrence, is independently selected from H, F, Cl, Br, I, CF₃,

C₃-C₆ carbocycle substituted with 0-3 R^{4b},

phenyl substituted with 0-3 R^{4b}, or

5 to 6 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-3 R^{4b};

R^{4b}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO₂, NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(=O)CH₃, S(=O)₂CH₃, C₁-C₄ alkyl, C₁-C₃ alkoxy, C₁-C₂ haloalkyl, and C₁-C₂ haloalkoxy;

R⁵ is H, OR¹⁴;

C₁-C₄ alkyl substituted with 0-3 R^{5b};

C₂-C₄ alkenyl substituted with 0-3 R^{5b};

C₂-C₄ alkynyl substituted with 0-3 R^{5b};

R^{5a} is H, methyl, ethyl, propyl, or butyl;

R^{5b}, at each occurrence, is independently selected from:

H, methyl, ethyl, propyl, butyl, CF₃, OR¹⁴, Cl, F, Br, I, =O;

C₃-C₆ carbocycle substituted with 0-3 R^{5c};

phenyl substituted with 0-3 R^{5c}; or

5 to 6 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-3 R^{5c};

R^{5c}, at each occurrence, is independently selected from H, OH, Cl, F, Br, I, CN, NO₂, NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(=O)CH₃, S(=O)₂CH₃, C₁-C₄ alkyl, C₁-C₃ alkoxy, C₁-C₂ haloalkyl, and C₁-C₂ haloalkoxy;

U.S. Appl. No. 09/505,788

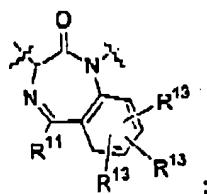
Response to Office Action Mailed 12/12/02

Page 86 of 93

R⁶ is H;

R⁷, at each occurrence, is independently selected from H, F, CF₃, methyl, and ethyl;

Ring B is



R¹¹ is selected from

H, C₁-C₄ alkoxy, Cl, F, NR¹⁸R¹⁹, C(=O)R¹⁷, C(-O)OR¹⁷, CF₃;

C₁-C₆ alkyl optionally substituted with 0-3 R^{11a};

C₆-C₁₀ aryl substituted with 0-3 R^{11b};

C₃-C₆ carbocycle substituted with 0-3 R^{11b}; or

5 to 6 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-3 R^{11b};

R^{11a}, at each occurrence, is independently selected from H, C₁-C₄ alkyl, OR¹⁴, F, =O, NR¹⁵R¹⁶, CF₃, or phenyl substituted with 0-3 R^{11b};

R^{11b}, at each occurrence, is independently selected from H, OH, Cl, F, NR¹⁵R¹⁶, CF₃, C₁-C₄ alkyl, C₁-C₃ alkoxy, C₁-C₂ haloalkyl, and C₁-C₂ haloalkoxy;

Z is C₁-C₄ alkyl substituted with 1-3 R¹²;

C₂-C₄ alkenyl substituted with 1-3 R¹²;

C₂-C₄ alkynyl substituted with 1-3 R¹²;

C₆-C₁₀ aryl substituted with 0-4 R^{12b};

C₃-C₆ carbocycle substituted with 0-4 R^{12b}; or

U.S. Appl. No. 09/505,788
Response to Office Action Mailed 12/12/02
Page 87 of 93

5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 6 membered heterocycle is substituted with 0-3 R^{12b};

R¹², at each occurrence, is independently selected from
C₆-C₁₀ aryl substituted with 0-4 R^{12h};
C₃-C₆ carbocycle substituted with 0-4 R^{12b}; or
5 to 10 membered heterocycle containing 1 to 4 heteroatoms selected from nitrogen, oxygen, and sulphur, wherein said 5 to 10 membered heterocycle is substituted with 0-3 R^{12b};

R^{12b}, at each occurrence, is independently selected from
H, OH, Cl, F, NR¹⁵R¹⁶, CF₃, acetyl, SCH₃, S(-O)CH₃, S(=O)₂CH₃, C₁-C₄ alkyl, C₁-C₃ alkoxy, C₁-C₂ haloalkyl, and C₁-C₂ haloalkoxy;

R¹³, at each occurrence, is independently selected from
H, OH, C₁-C₆ alkyl, C₁-C₄ alkoxy, Cl, F, Br, I, CN, NO₂, NR¹⁵R¹⁶, and CF₃;

R¹⁴ is H, phenyl, benzyl, C₁-C₄ alkyl, or C₂-C₄ alkoxyalkyl;

R¹⁵, at each occurrence, is independently selected from H, C₁-C₄ alkyl, benzyl, phenethyl, (C₁-C₄ alkyl)-C(=O)-, and (C₁-C₄ alkyl)-S(=O)₂-;

R¹⁶, at each occurrence, is independently selected from
H, OH, C₁-C₄ alkyl, benzyl, phenethyl,
(C₁-C₄ alkyl)-C(=O)-, and (C₁-C₄ alkyl)-S(-O)₂-;

R¹⁷ is H, methyl, ethyl, propyl, butyl, methoxymethyl, ethoxymethyl, methoxyethyl, ethoxyethyl,
phenyl substituted by 0-3 R^{17a}, or
-CH₂-phenyl substituted by 0-3 R^{17a};

R^{17a} is H, methyl, methoxy, -OH, F, Cl, CF₃, or OCF₃;

U.S. Appl. No. 09/505,788
Response to Office Action Mailed 12/12/02
Page 88 of 93

R¹⁸, at each occurrence, is independently selected from
H, methyl, ethyl, propyl, butyl, phenyl, benzyl, and phenethyl; and

R¹⁹, at each occurrence, is independently selected from
H, methyl, and ethyl;

provided, when R¹³ is H,
then Z is butyl substituted with 1-3 R¹²;
C₂-C₄ alkenyl substituted with 1-3 R¹²; or
C₂-C₄ alkynyl substituted with 1-3 R¹².

63. (NEW) A pharmaceutical composition comprising a compound according to Claim 57 and a pharmaceutically acceptable carrier.

64. (NEW) A pharmaceutical composition comprising a compound according to Claim 58 and a pharmaceutically acceptable carrier.

65. (NEW) A pharmaceutical composition comprising a compound according to Claim 59 and a pharmaceutically acceptable carrier.

66. (NEW) A pharmaceutical composition comprising a compound according to Claim 60 and a pharmaceutically acceptable carrier.

67. (NEW) A pharmaceutical composition comprising a compound according to Claim 61 and a pharmaceutically acceptable carrier.

68. (NEW) A pharmaceutical composition comprising a compound according to Claim 62 and a pharmaceutically acceptable carrier.

69. (NEW) A method for the treatment of Alzheimer's Disease comprising administering to a host in need of such treatment a therapeutically effective amount of a compound of Claim 57.

U.S. Appl. No. 09/505,788
Response to Office Action Mailed 12/12/02
Page 89 of 93

70.(NEW) A method for the treatment of Alzheimer's Disease comprising administering to a host in need of such treatment a therapeutically effective amount of a compound of Claim 58.

71. (NEW) A method for the treatment of Alzheimer's Disease comprising administering to a host in need of such treatment a therapeutically effective amount of a compound of Claim 59.

72. (NEW) A method for the treatment of Alzheimer's Disease comprising administering to a host in need of such treatment a therapeutically effective amount of a compound of Claim 60.

73. (NEW) A method for the treatment of Alzheimer's Disease comprising administering to a host in need of such treatment a therapeutically effective amount of a compound of Claim 61.

74.(NEW) A method for the treatment of Alzheimer's Disease comprising administering to a host in need of such treatment a therapeutically effective amount of a compound of Claim 62.